Partial Gastrectomy

Complications and Metabolic Consequences

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1

INTRODUCTION

F. A. R. Stammers

One of the major maladies of civilized countries is peptic ulcer; there is evidence that its incidence throughout the world increases with an expanding economy and an increasing tempo of life, although in the older civilizations of Western Europe there is a suggestion that the incidence may be on the decline. Susser and Stein (1962), studying the incidence of peptic ulcer over the last half century, state that when treated on the cohort basis it would seem that each generation carries its own risk, and that in later generations peptic ulcer is on the decline and can no longer be regarded as a disease of civilization. During recent visits to the Sudan (in 1961), and Southern Rhodesia (in 1962) I was informed by various members of the Health Services in those countries that peptic ulcer was very definitely on the increase. Doll, Avery Jones and Buckatzsch (1951) calculated that, in Great Britain at any one time there were about 700,000 people suffering from the acute phase of such an ulcer. Each year, probably not more than about 5 per cent of these cases require surgery, since the majority are kept comfortable by simple dietetic and medicinal means. In the days when the operative mortality rate for partial gastrectomy, and for the simpler operations too, such as gastro-enterostomy, was anything between 8 and 12 per cent physicians were naturally hesitant in suggesting surgical intervention and tended to adopt the attitude of protecting their patients from operation, except for perforation or repeated incidents of bleeding. As one eminent physician of those days put it 'the patient must learn to live with his ulcer and keep it in subjection. If he is not prepared to do this, he must pay the penalty of an operation.' Ogilvie (1952), on the other hand, said 'the only safe course is to advise gastrectomy in all ulcers that are not rapidly and permanently healed by rest and diet. We can do this without hesitation because we know that the patient will live happily ever afterwards.' The truth does not quite reach the latter situation even now but is steadily approaching it.

Certainly in my own early days, the average case referred to me by medical colleagues had suffered symptoms for anything from

10 to 20 years, often having been in hospital under medical care on several occasions, rarely remaining free from pain subsequently for more than 6–12 months, progressively losing more and more time from work, and not infrequently developing complications such as anaemia, malnutrition, bleeding or signs of stenosis. Heuer (1944) reporting on 732 cases treated medically up to 1942 concluded that little more than 50 per cent of patients were cured by conservative treatment; Evans (1954), based on 111 cases, said the same; and Martin and Lewis (1949) reviewing, after World War II, 356 cases of peptic ulcer admitted to the medical wards of Addenbrooke's Hospital during the five-year period 1934–38, were able to trace 337, of whom 195 were still living; the subsequent history and cause of death in the remaining 142 were ascertained. They came to the conclusion that medical treatment did not appear to influence the natural course of the disease.

The physician of today turns to his surgical colleague much more readily because the necessary operations are so much safer since the advent of better anaesthesia, readily available blood, better understanding of fluid and electrolyte balance, and chemotherapy. Up to the present time it has been difficult to ascertain how many partial gastrectomy operations for peptic ulcer are carried out in Great Britain each year, but now that statistical information is collected from hospitals in England and Wales for the Hospital In-patient Enquiry, information of this kind is becoming available. The Registrar General states that in England and Wales in 1956 an estimated 71,800 cases of peptic ulcer were discharged from hospital, of whom 34,800 received surgical treatment. Of these operations 22,600 were partial gastrectomies, the remainder being mostly vagotomies, gastro-enterostomies or simple suture for perforation.

Until about fifteen years ago the general principles of surgical treatment were to excise the ulcer bearing area and to reduce the production of acid and pepsin by removing a major part of the stomach; this varied from 60 to 90 per cent, the smaller amount usually being for gastric ulcer and the larger for duodenal ulcer. Reconstruction was by gastro-jejunostomy for duodenal ulcer (Billroth II, commonly referred to as the Polya operation) or by gastro-duodenostomy for gastric ulcer (Billroth I) (*Figure 1*). For duodenal ulcer an even earlier group of surgeons performed no more than simple gastro-enterostomy, believing that this was a much safer procedure and equally effective. However, the high incidence of subsequent anastomotic ulceration proved to be a serious disadvantage.

There have been so many modifications of Billroth's original two patterns of partial gastrectomy—reconstructing by joining the stomach stump to the duodenum in the first one, and to the jejunum, in the second—that considerable confusion has arisen as to what precisely is meant by the operations associated with the names of Kronlein, Eiselsberg, von Harberer, von Hacher, Polya, Moynihan, Pauchet, Finisterer, Mayo, Balfour, etc. For instance, many surgeons when referring to the Polya operation, mean partial gastrectomy with reconstruction by either ante- or retro-colic gastro-jejunostomy; the true Polya was, of course, retro-colic (1911). For this reason, and because Billroth was the great pioneer of gastric surgery, the expressions Billroth I or Billroth II will be used to mean partial gastrectomy with reconstruction by gastro-duodenostomy or by gastro-jejunostomy, respectively. For the latter operation the further

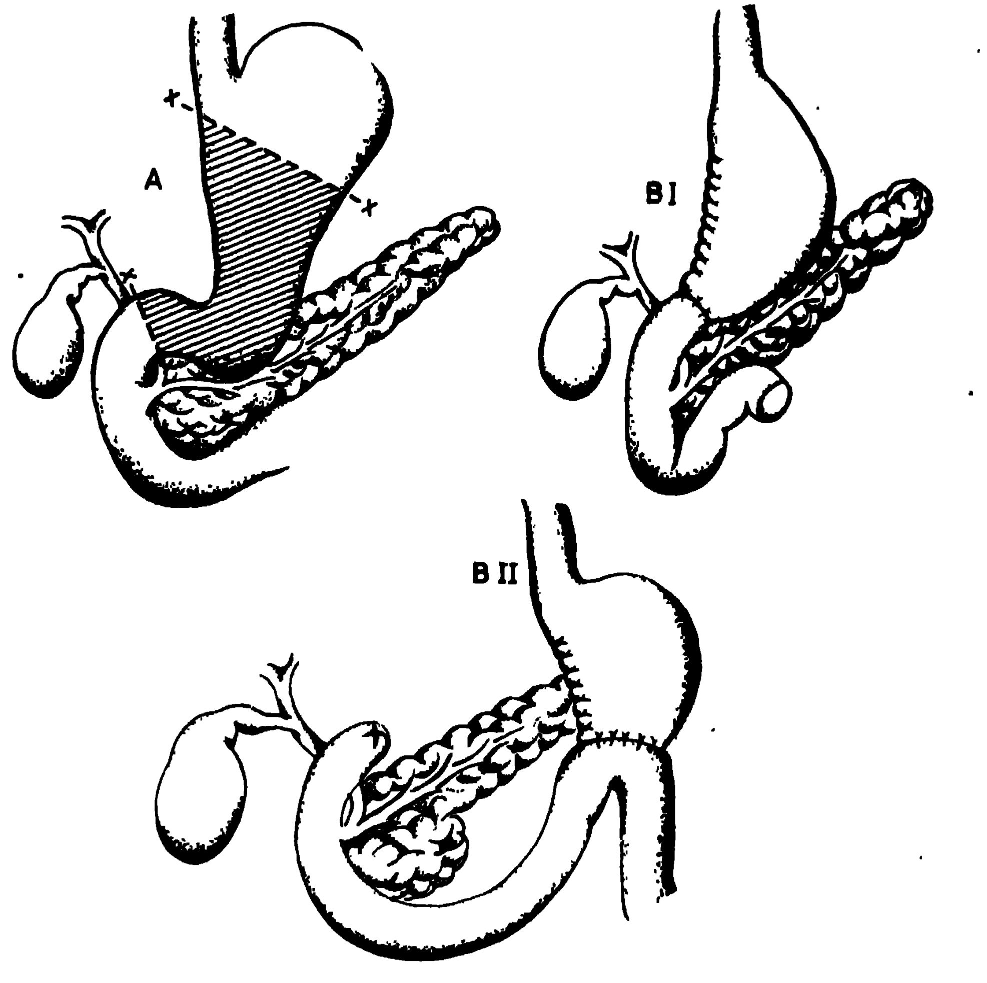

Figure 1. Partial gastrectomy with removal of 75 per cent of the stomach (A); *reconstruction by gastro-duodenostomy—Billroth I*—(BI); *or by gastro-jejunostomy—Billroth II*—(BII)

descriptions 'retro-colic' or 'ante-colic', or of 'afferent loop to lesser curve' or 'afferent loop to greater curve' may be added. I shall not mention the matter of a valve (Hofmeister) since in our own series it seemed to make no difference regarding results (Brookes, Waterhouse and Thorn, 1960).

Many surgeons felt unhappy about these major gastrectomies of more than 75 per cent as advocated, soon after World War II, by the authorities of the day (Finisterer, Morley, Balfour, Ogilvie), especially in young people, or in those suffering from phthisis; this anxiety attracted them to Dragstedt's experimental work (1943) and his re-introduction of vagotomy. Since then there has been much re-thinking concerning the whole problem of peptic ulcer. This has been stimulated by the publication of an increasing number of carefully followed-up series from different areas and by individual surgeons which show that, quite apart from operative mortality, there is a remarkably constant failure rate after partial gastrectomy of about 10 per cent; and 10 per cent of almost 23,000 per annum forms a considerable body of dyspeptic invalids, disappointed, worried and losing time from work—in fact, a national liability. Multiply this by the number of years since the war, and it becomes a formidable problem.

The object of this book is to suggest ways and means of reducing immediate post-operative complications including death, and of minimizing the incidence of post-gastrectomy problems. It is based

TABLE 1

Analysis of 79 Cases of Post-gastrectomy Complications

(a) *Immediate post-operative* (18)

Predominant lesion	*Number*	*Result*
Torsion at stoma with obstruction	2	Both recovered
Leak of duodenal stump	3	1 recovered; 2 died
Anastomotic leak	1	Recovered
Pancreatitis	2	Both died
Entero-colitis	1	Recovered
Omental inflammatory reaction	2	Both recovered
Reactionary haemorrhage at anastomosis	1	Recovered
Obstruction at stoma by adherent lig. teres	1	Recovered
Obstruction at stoma by bezoa	1	Recovered
Loop-the-loop obstruction	3	Recovered
Injury to middle colic artery—subsequent gangrene of colon	1	Died

TABLE 1 (*contd.*)

(b) *Early or delayed* (61)

Predominant complaint	*Number*	*Result*
Leaking Bancroft operation (see p. 40)	1	Well
'Little stomach' syndrome	1	Well
'Dumping syndrome'	5	All 5 much better
Steatorrhoea	6	4 well; 1 fairly well; 1 died

(c) *Delayed*

Steatorrhoea with osteomalacia	2	Both better
Stomal ulcer	17	8 well 3 fairly well 3 died (renal failure; carc. bronchus; sub-arachnoid haemorrhage) 1 'dyspeptic wreck' 1 emigrated 1 untraced
Gastro-colic fistula	2	Both well
Afferent loop syndrome (including concertina'd afferent loop)	12	6 well 3 continued dyspepsia 1 crippled with bronchitis 2 died (ca. stomach; ca. bronchus)
'Obstruction-en-coccoon'	8	7 well 1 died
Food obstruction	2	1 well 1 dyspepsia continued
Chronic abdominal wall abscess	1	Well
Psychological instability	4	1 killed in road accident 3 alive but dyspepsia continues

on a special study of two different groups of patients. The first group consists of 79 cases of post-gastrectomy complications, 18 of which developed during the immediate post-operative period and were therefore all personal cases; 61 consisted of one or other of the so-called post-gastrectomy syndromes or other delayed complications. Of the latter figure, 23 were from our own series and 38 were referred from other hospitals (Table 1). The second study concerned another group of our total series and concentrated on certain metabolic features which may follow partial gastrectomy, with special reference to iron, iron-binding capacity, vitamin B_{12}, fat, protein and calcium; the latter group amounted to 250 patients.

A background to all this work is our continued follow-up of over 1,000 cases of partial gastrectomy for peptic ulcer carried out by different members of the Surgical Professorial Unit in Birmingham.

Finally, as a result of these studies, certain conclusions are drawn and suggestions made for a different approach to the surgical treatment of peptic ulcer. The book contains a review of general results reported from major centres and discusses the selection of patients for surgical treatment, preparation for operation and early post-operative care with special reference to complications developing during the immediate post-operative period. The post-gastrectomy syndromes and other delayed complications are reviewed and examples are given from our own cases. Some of these syndromes, such as that due to afferent loop obstruction, are largely of mechanical origin and present with gastro-intestinal symptoms, while others, such as 'dumping', are partly mechanical and partly metabolic in nature. In some cases several mechanical factors are operative at the same time, perhaps with associated metabolic disturbances giving a somewhat confused picture. A clinical approach to these problems and their analysis is suggested and their treatment is discussed. Another group of phenomena is being recognized, features of which are essentially metabolic in origin such as anaemia or malnutrition, which may be entirely devoid of gastro-intestinal symptoms and so may not be suspected as being connected with the operation. An account of these metabolic consequences of partial gastrectomy is described in Chapters 6–11. It includes studies of gastric and jejunal biopsies and gives details of a simple technique for obtaining bone biopsies, suitable for use on out-patients. All such investigations add greatly to the knowledge of the physiology of digestion, and we have now reached the exciting stage when we can study the physiology of human digestion in man himself. We are still far from knowing the full facts, but the latest understanding of the problem is given in Chapter 5. It is important that surgeons be familiar with new viewpoints, since partial gastrectomy changes the anatomy, and therefore physiology, in so fundamental a manner.

Sometimes nature performs her own experiments which bring to light unexpected phenomena, with or without gastro-intestinal symptoms. Such experiments are usually of a mechanical kind as, for instance, that over the course of years following partial gastrectomy gradual embarrassment of afferent or efferent loop is produced, resulting in symptoms of which some are a reflection of metabolic disturbance, e.g. dumping; on the other hand, such an experiment may lead to the accentuation of some pre-existing, but hitherto symptomless, variation from normal, sprue and coeliac disease being examples. Observations of this kind are valuable, despite the much greater number of variables—chiefly psychogenic—that there are in man as compared with animals, because they help to translate to human mechanisms the results of animal experiments. An attempt is made to interpret these experiences, and to see whether they point to a more rational approach to the surgical treatment of peptic ulcer.

It is not proposed to describe the technical details of the different operations for peptic ulcer since these are adequately dealt with in standard textbooks (Grey-Turner and Rogers, 1955; Maingot, 1953; Shackleford, 1955); we shall refer to those points of technique which, if disregarded or wrongly executed, may lead to trouble, however.

A REVIEW OF THE CHANGING RESULTS OF PARTIAL GASTRECTOMY

Since World War II a general improvement in mortality rates for all operations has taken place, and this is mainly because the experience of war surgery made all surgeons more aware of the fundamental importance of fluid and electrolyte balance, how to recognize imbalance and how to correct it. With this experience grew an alertness concerning delayed shock and how to prevent it, recognizing hypovolaemia, often from blood loss, as the essential factor. It also showed the way towards effective methods of correcting nutritional deficiencies. At the same time, the new school of thoracic surgeons lead to a much better appreciation of the importance of the care of the bronchial tree, especially in the elderly bronchitic. Modern anaesthetics, readily available blood and antibiotics have already been mentioned, and it is important to keep in mind all these points when comparing different series and to note their dates since—assuming equality of hospital size and availability of ancillary services—a series between 1945 and 1955 should show better results than one of the same size 15 years earlier.

A group of reports from well-known centres in the U.S.A. appeared in 1930, when duodenal and gastric ulcers were usually grouped together as one disease. For instance, Horsley reported a mortality rate of 7·5 per cent for partial gastrectomy in 160 cases of peptic ulcer; Gibbon as 10·8 per cent; and Finney and Hanrahan as 12·9 per cent; the latter stated that their mortality for simple gastro-enterostomy was 8·1 per cent. They also recorded that for all forms of surgical treatment of duodenal ulcer it was 7·1 per cent in 339 cases, and for gastric ulcer 9·7 per cent in 268 cases. It is unfortunate that many papers from Great Britain on the subject, and covering the same period, often gave no figures at all.

Moving on another decade, Lake (1948) reviewed 615 personal cases of gastrectomy, 525 being for benign ulcers including stomal ulcer, and reported a mortality of 5·7 per cent; these figures embrace both duodenal and gastric ulcers. Another interesting though smaller series is that recorded by Watson (1947) in which he makes special reference to the post-operative developments of anaemia. Regarding post-gastrectomy problems, it is important to observe patients for an adequate time, since most series show that a small proportion of 'cures' have stepped down into a less satisfactory category 5–7 years later because of the development of some such trouble as stomal ulcer or anaemia. Others, however, at first not quite free from discomforts such as diarrhoea or dumping, improve. The question of whether or not to follow-up patients is always a vexed one, and some medical men feel that such interviews instil into the minds of these people a sense of continued invalidism; it goes without saying that any follow-up must be by personal interview. Certainly the way questions are put influences the answers obtained, so that the surgeon who greets his patient with a jovially-expressed presumption that he has never suffered the slightest discomfort since leaving hospital is likely to get the answer he wants; whereas the super-conscientious observer who positively flagellates himself with such questions as 'do you never get any pain; do you really mean to tell me that you never have the slightest suspicion of fullness, or faintness, or heartburn, or diarrhoea' will almost certainly sap such confidence as the patient had when he first entered the room. The subjective feelings of the patient are a good indication of success or failure of the operation yet, today, in view of the figure of 10–12 per cent failures already mentioned, some follow-up clinics such as our own are trying to discover the genesis of such metabolic changes as anaemia, failure to gain weight, steatorrhoea, etc., and so employ more objective investigations, such as blood studies, estimations of serum-iron, iron-binding capacity, serum B_{12}, jejunal biopsy, faecal fat and, more recently, bone biopsy. The patient should be reassured by explaining to him the scientific objective behind these tests. We have done this during the past few years in Birmingham, and the results are reported in Chapter 11.

In 1956, Thorn, Brookes and Waterhouse followed-up the 955 patients treated for peptic ulcer by the different members of the Surgical Professorial Unit in Birmingham, with the object of ascertaining whether there was a greater incidence of pulmonary tuberculosis in these patients than in the general population; these findings are mentioned on p. 100. They also took the opportunity of analysing the results in general (1960), which I will now quote.

The total number of cases was 955, of which 79 were known to be dead, thus leaving 876. Of these, 826, i.e. 94·3 per cent of the whole, were actually interviewed and examined. Operative mortality for the whole was 3·87 per cent, but there was considerable variation according to age (see Table 2).

TABLE 2

Age years	*Total cases*	*Number of deaths*	*Mortality rate* per cent
Under 44	342	5	1·46
45-54	343	10	2·92
55-64	212	14	6·6
Over 65	58	8	13·8

With respect to type of operation, 828 were gastro-jejunostomies (Billroth II) of which 725 were ante-colic operations, and 103 were retro-colic operations, both having afferent loop to lesser curve and about one-third having Hofmeister valves; gastro-duodenostomy (Billroth I) was used in 127 cases. The amount of stomach removed in both groups varied from 50 to 90 per cent. With regard to results, 65·4 per cent were able to lead a normal life and had no symptoms of any significance; a further 22·6 per cent were also able to lead a normal life, although they had to take certain precautions, such as avoiding tough food or unripe fruit and, in some cases, taking alkalis; the remaining 10 per cent still complained of various forms of dyspepsia, although 42 of this group, 5·1 per cent of the whole, said that they were not wholly dissatisfied with the operation since they had lost their original ulcer pain. The complaints of the 10 per cent consisted of such things as bilious vomiting, faintness and sweating, abdominal discomfort after meals, diarrhoea, sometimes with features of steatorrhoea, loss of weight, and the symptoms of stomal ulcer or of anaemia. So far as the latter is concerned, and based on haemoglobin levels only, 8·5 per cent of men and 5·9 per cent of women so suffered. There were 38 instances of bilious vomiting and only 15 of stomal ulcer.

During 1955-60 the unit performed a further 354 partial gastrectomy operations for simple peptic ulcer with a mortality of 1·4 per cent, two patients being over 55 years of age.

Many of the post-gastrectomy failures described in this work were, as already explained, referred from other centres, and so were not included in the analysis by Brookes, Waterhouse and Thorn (1960). This book deals with the management and follow-up of these complications, and since embarking upon it we have operated on a further 16 cases, generally finishing by conversion to a Billroth I type of reconstruction plus vagotomy. The results are most promising, but it is felt that the follow-up time is too short to include them here.

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2

PREPARATION FOR OPERATION AND POST-OPERATIVE CARE

F. A. R. Stammers

Every operation has its potential complications—including death. Some of these are of a general nature, such as cardiac, pulmonary, renal or thrombotic; some are local according to the particular region involved, such as peritonitis, abscess formation or intestinal obstruction, and some are peculiar to the particular operation concerned, such as duodenal stump leakage. Much can be done to prevent complications of a general nature by careful pre-operative preparation; indeed, hope of yet further reduction in mortality lies very largely in this direction, particularly now that an increasing number of older people become candidates for operation. At the same time, a growing appreciation of the danger points of technique and how to circumvent them, and also a more carefully planned programme of pre- and post-operative care, play their part in improving results and preventing later complications.

One can refer to this preparation for operation as the establishment of a state of physiological balance in all systems; in other words, by full investigation and appropriate treatment to befit the patient for his operation by getting him into as near normal constitutional condition as possible.

Of course, many patients—perhaps the majority—are already in physiological balance at the time of admission to hospital as, for instance, the young man with a hernia, the schoolboy with a fractured clavicle or acute appendix, and even the majority of patients with duodenal ulcer; the necessary surgical treatment for all these conditions may confidently be expected to be successful and without incident. In constitutionally fit people, relatively minor complications such as wound sepsis, venous thrombosis or collapse of part of one lung will almost certainly be surmounted with little difficulty. Should there be some pre-existing disorder, such as emphysema, chronic bronchitis, cardiac or renal disease, however, the complications mentioned might well prove serious, even fatal. Such states should, of course, be easily recognized during general examination, but mild degrees of metabolic disturbance, such as dehydration, salt depletion, hypoproteinaemia (rare in Great Britain), avitaminosis or mild anaemia, all of which may be associated with long-standing peptic ulceration, may remain unsuspected unless deliberately looked for. If uncorrected, these abnormalities tend to interfere with the defensive mechanisms of the body against complications such as sepsis, to hinder convalescence in such ways as delayed wound healing, and to cause a slowing-up of return of appetite, energy, and feeling of well-being.

It is clear, therefore, that if the best results are to be obtained, the surgical management of peptic ulcer should be undertaken only in fully-equipped hospitals with adequate resident medical and nursing staff and emergency services for clinical pathology and radiology; a physiotherapy department is also a great asset. Unfortunately, some hospitals do not possess all these amenities, so that pre-operative investigations tend to be confined to clinical examination, urine testing, x-ray studies and haemoglobin estimations; and there may be incomplete assessment of the precise condition of the patient and delay in early recognition of an impending complication because of the absence of the necessary services after 5 p.m.

With respect to the chest, many patients have coughs when first seen—some no more than a smoker's cough, others with long-standing bronchitis, bronchiectasis or even tuberculosis, some with pneumoconiosis associated with working in dust, and still others who have suffered some acute respiratory infection during adult life. The effects of anaesthetics on the chest can be minimized by insisting that the patient gives up smoking and by establishing breathing exercises, including postural drainage, under the supervision of a physiotherapist in order to clear the bronchial tree of retained secretions. Up to a few years ago many surgeons prescribed penicillin as routine before operation if bronchial secretions were discovered to be infected, but in view of the problem of resistant organisms and cross-infection in hospitals, as well as the fact that it does not prevent chest complications, the policy now is to avoid antibiotics unless post-operative chest complications arise, and then to prescribe according to the sensitivity of the organisms, and to give two antibiotics at a time. The problems of pulmonary tuberculosis are dealt with on p. 100.

The large bowel should be cleared before operation especially when barium studies have been made, because this barium may form hard masses in the colon which can cause discomfort during the first few days after operation.

If there is any suspicion of heart disease, as suggested by breathlessness, pain in the chest on exercise, swelling of the ankles, recurrent bronchitis or by irregularity of the pulse or fullness of neck veins, a specialist opinion should be obtained.

The state of the renal tract should be ascertained and, in older men, prostatic enlargement must always be suspected, since it may lead to urinary retention which, in turn, may lead to subsequent infection. If residual urine is less than 60 ml, and provided the urine is uninfected, there is no need to do more than watch for further retention during convalescence, but if there is retention in excess of 60 ml, renal function should be investigated. Infection of the urinary tract or defective renal function must be treated before embarking on any surgical procedure for peptic ulcer; but even in the absence of these, retention means that treatment of the prostatic enlargement must be considered seriously first. Reference to haemorrhage from the ulcer following prostatectomy is made on p. 24.

The dehydration due to vomiting in an established pyloric stenosis is self-evident but where, during the previous few weeks, there has been only occasional vomiting in smaller quantities, it is wise, especially in patients over 50 years of age, to measure serum electrolyte levels. A relatively good colour may be deceptive, and pink mucous membranes may result from haemo-concentration hiding a real anaemia. Victims of long-standing peptic ulcer are liable to restrict their diet so severely as to deprive themselves of meat, fruit and green vegetables, and so be deficient in vitamins. It was once thought that protein deficiency might also result but investigation shows that even on milk diet this is rare, unless due to liver failure. Investigations for vitamin C deficiency will reveal any abnormality, which should be corrected before operation. The majority of patients will be in balance but, in the elderly, deviations from normal are not uncommon.

It is necessary to arrange for two half litre bottles of blood to be available in anticipation of possible losses during operation. Where the operation is for an actively bleeding ulcer, or a second or third operation for one of the post-gastrectomy syndromes where separation of adhesions will cause oozing, four or five bottles may be needed. Hypotension is especially liable to follow blood loss in the elderly, and such loss as may occur should be made good during the operation.

A history of venous thrombosis following a previous operation is a warning that every device for preventing its recurrence needs to be taken, including the pre- or immediately post-operative use of anticoagulants. Care should be taken not to allow pressure on the calves of the legs during operation, and in all cases patients should be encouraged to move the legs in bed from the beginning; early ambulation is also important. When in doubt, a daily inspection of the legs should be made for early signs, such as slight oedema, tenderness of the calf or Homans' sign, although, as the work of Sevitt and Gallagher (1961) has shown, mural clots may be present in the deep femoral or pelvic veins without any such signs. Prevention is more important than early detection.

POST-OPERATIVE CARE

The maintenance of physiological balance is of vital importance during the immediate post-operative period and prevents a number of complications. The exact régime used varies in different centres, but most will establish gastric suction and intravenous fluids before, during or after operation. Some surgeons argue that a stomach tube of any sort is uncomfortable for the patient and not altogether free from complications, such as irritation of the pharynx or regurgitation which may lead to inhalation of gastric contents or, more rarely, to an inflammatory reaction in the lower end of the oesophagus resulting in stenosis; the latter is referred to on p. 56. From time to time, correspondence appears in the journals on 'tubeless gastric surgery', a recent one being initiated by the paper of Hendry (1962). Enthusiasts maintain that naso-gastric tubes are necessary in only 1–2 per cent of cases, and that patients are much more comfortable without them. Bevan (1961) showed that, in a patient with such a tube, its removal improved measured pulmonary function by up to 24 per cent. However, nobody knows how to foretell the 1 or 2 per cent who, for some reason or other, will develop gastric retention; in reconstruction operations, particularly for some of the complications about to be described, the stomach stump tends to remain inert for longer than after primary operations for ulcer. I entirely agree with those who say that naso-gastric tubes should be removed after 12–24 hours, unless there is evidence of excessive aspiration. Because of these complications some American centres use gastrostomy drainage instead of a naso-gastric tube.

The employment of tubes by either route reduces the risk of vomiting and thereby inhalation of vomit, shows up any reactionary bleeding, prevents gastric retention and thus tension on suture lines which this might cause, and minimizes the risk of that rare, though much more dangerous, condition of acute dilatation of the stomach. Where gastric suction and intravenous therapy are used a fluid balance chart must be kept accurately from the start. As a simple guide it is true to say that, for our climate, a patient wholly dependant on parenteral fluids and with no abnormal losses requires 2½–3 l./day; in tropical countries 3–4 l., or even up to 5 l., are necessary, since the loss by sweating is much greater. Admittedly, a high proportion of patients in physiological balance prior to operation can tolerate 2–3 days' starvation and low fluid intake, since the natural response of the body to operation, through the supra-renal cortex, is retention of salt and water, and for this reason some surgeons do not give intravenous therapy as a routine. Nevertheless, if some complication makes it necessary to withhold fluids for longer than average, the patient then faces the situation at a disadvantage and in the elderly this may spell disaster.

My own post-operative régime is to allow nothing by mouth for the first 12 hours, 25 ml water hourly for the next 12 hours, followed by 50 ml/h for the next 12 hours, followed again by 75 ml/h for a further 12 hours. At the same time, the patient receives intravenously about 2,500 ml during the first 24 hours and 2,000 ml during the second, the lesser amount being offset by that retained by mouth. These fluids vary between saline, glucose and Darrow's solutions, the electrolytes amounting to about 60 mequiv. potassium and 150 mequiv. sodium per day. Where there has been blood loss during operation the blood drip should be continued until the estimated loss is replaced. Haemoglobin and packed-cell volume estimations may be necessary because there is no simple way of measuring the amount lost during operation, although an approximation can be made by the methods described by Clarke and Fisher (1956). From time to time, however, more is lost than is appreciated or internal haemorrhage continues, and only when the patient collapses is this realized. As already stated, blood loss should never remain uncorrected.

Urine output is carefully recorded and should be about 1,000 ml/day; anything less is a warning to check on fluid and electrolyte levels.

During the first 24–48 hours aspiration is applied immediately before each hourly drink in order to check on any gastric retention and, incidentally, to note if there is blood therein. Although the planned total intake should be adhered to, double quantities may be given two-hourly instead of hourly, again preceded by aspiration, provided that the patient is comfortable and that there is no evidence of intra-gastric accumulation. When the hourly intake has reached 100 ml the drip can be stopped, and when bowel sounds have returned, caloric intake by mouth can be increased by starting a light diet.

Intestinal movements are always reduced by abdominal operations, and bowel sounds are damped down during the first two or three post-operative days. It is wise to try to establish a bowel action on the third day; suppositories have largely replaced enemata and are less disturbing to the patient and time-saving to the nursing staff.

The other important routine treatment, almost from the moment of return to consciousness, is breathing and coughing exercises, often with positioning and preferably under the supervision of a physiotherapist. There is no doubt that this, combined with early ambulation, has substantially reduced the seriousness of chest complications. Early ambulation also minimizes the risk of venous thrombosis and is, at the same time, a psychological stimulus to the patient.

SUMMARY

Improvement in the results of operation for peptic ulcer depends on choice of case and respect for the establishment and maintenance of physiological balance. This includes a general assessment of the nutritional state and its correction before operation where possible; all are of particular importance in the elderly but such investigations demand adequate laboratory services. The immediate post-operative phase requires continued care regarding fluid and electrolyte balance and particular attention to the bronchial tree. Early ambulation is important.

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3

IMMEDIATE POST-OPERATIVE COMPLICATIONS

F. A. R. Stammers

As already stated, immediate post-operative complications may be divided, first, into those of a general nature liable to follow any surgical intervention, particularly abdominal operations and, secondly, into those peculiar to gastric surgery. The causes of death following operations on the stomach and duodenum are well demonstrated by the paper of Marshall and Reinstine (1957), reporting on 254 cases between 1932 and 1954 (see Table 3).

TABLE 3

Cause	*With autopsy*	*Without autopsy*
Sepsis: Peritonitis (39) Localized (2) Lung abscess (6) Sub-diaphragmatic (3)	50	24
Pneumonia	21	18
Pulmonary embolus	12	9
Cardiac	10	15
Metabolic	10	20
Shock	8	16
Pancreatitis	7	2
Uraemia	6	4
Intestinal obstruction	0	3
Undetermined	12	7
Total	136	118

In order to collect adequate numbers for comparison we have studied the post-mortem reports on post-operative deaths following partial gastrectomy throughout both Teaching Hospitals in Birmingham, covering the years 1952–61. They amount to 112 and, although 20–30 years later than Reinstine's series, they form a remarkably similar pattern. It shows, also, that leaking duodenal stump or anastomotic line is still a common cause of peritonitis (see Table 4, based on similar classification to Table 3).

TABLE 4

Cause		*With autopsy*
Sepsis	Peritonitis	35
	Localized	1
	Lung abscess	2
	Sub-diaphragmatic	0
Pneumonia		26
Pulmonary embolus		15
Cardiac		10
Metabolic		0
Shock		2
Pancreatitis		0
Uraemia		2
Intestinal obstruction		4
Mesenteric infarction		2
Ileus		4
Torn spleen—bleeding		1
Entero-colitis		4
Cerebral embolism		3
Liver abscess		1
Total		112

Analysis of causes of peritonitis in 35 cases:

Leaking duodenal stump	10
Leaking anastomosis	13
Undetermined (possibly contamination, probably leak)	12

POST-OPERATIVE COMPLICATIONS OF A GENERAL NATURE

Shock

The state of hypotension referred to as shock is related to hypovolaemia resulting from bleeding and loss of other fluid, although pain can aggravate it. With proper preparation shock is unlikely to develop during operation, except in the frail, elderly person where there has been either a steady loss of blood during separation of adhesions, or a more sudden one as, for instance, during the dissection of a posterior duodenal ulcer from the head of the pancreas, especially if adherent to the pancreatico-duodenal artery. A few instances of severe haemorrhage, often unrecognized, have been recorded resulting from a tear of the spleen where an atypical fold of peritoneum, attached to the periphery of its under-surface, has been stretched tightly by too firm a retraction. It is the persistent oozing from separated adhesions that is particularly dangerous, since its cumulative volume may not be appreciated until the anaesthetist calls attention to the relatively sudden fall in blood pressure, or even the disappearance of pulse; the best remedy is to give blood, plasma or dextran rapidly, e.g. 1 l. in 10 min. Should there be the least suggestion of heart arrest, external cardiac massage should immediately be applied. Hypotension developing during the first 24 hours after operation may again be due to hypovolaemia resulting from continued intra-abdomonal oozing. Any myocardial lesion, of course, renders the heart more liable to damage due to blood loss, and where there is anoxia, fibrillation may follow. Collapse of a major portion of one or both lungs will lead to further cardiac anoxia.

Heart Failure

This has already been discussed above. In spite of pre-operative investigations and preparation, failure occurs occasionally as a result of complications such as lung collapse followed by pneumonia, or the toxaemia associated with wound infection, peritonitis or intra-abdominal abscess. Blood pressure falls, pulse rate rises and becomes irregular, the limbs are cold and moist, sacral oedema may ensue and ileus may develop. It is especially important to observe electrolyte levels but, at the same time, to avoid an excess of intravenous fluids, since this may cause pulmonary oedema and throw further strain on the heart. It is in these cases that potassium is important since hypokalaemia may be partly responsible. Potassium balance is discussed on p. 46.

Pneumonia

A major premeditated operation should never be carried out within a few days of any upper respiratory infection. Following the operation, the usual course of events is lung collapse, resulting from bronchial obstruction by mucus or inhaled stomach contents, and then subsequent infection, and all this is more common in the chronic bronchitic (mention of the relationship of phthisis to gastrectomy is made on p. 100). At one time it was believed that dental sepsis contributed to the infection of collapsed lung or to the risk of wound sepsis, and that irreparable teeth should be extracted prior to any abdominal operation. It is now known, however, that multiple extractions lead to a bacteraemia lasting up to six weeks, during which time the patient is more vulnerable to the trauma of major surgery (Okell and Elliott, 1935; Round, Kirkpatrick and Hails, 1936). When relatively few teeth are affected, it is generally agreed that they should be removed reasonably soon after the main operation, but where severe pyorrhoea is extensive it is best to extract the affected teeth first and to postpone the gastric operation until three months later, unless some acute phase such as haemorrhage or pyloric stenosis dictates otherwise.

Following the operation, breathing and coughing exercises under the supervision of a physiotherapist are of major importance. The chest should be examined each day, and x-rayed when in doubt; if there is sputum, the bacteriology and sensitivity to antibiotics of the organisms should be established. Excessive sputum may suggest that the lungs are oedematous and care should be taken that an excess of intravenous fluid is not being given. Where simple methods are not effective, and especially in the case of an elderly patient, bronchoscopy and bronchial suction, or even tracheostomy in order to reduce dead space and to clear the bronchial tree, may be life-saving.

Bevan (1961), while working with us, showed that chest complications were more common after upper, than after lower, abdominal operations although there was no significant difference between vertical and horizontal incisions. He related these complications partly to the amount of air left in the abdominal cavity and strongly urged that an attempt should be made to extract it before tying the last few peritoneal stitches. Abdominal distension and the supine position contributed to chest complications by diminishing vital capacity and reserve air.

Thrombosis and Risk of Pulmonary Embolism

This is no more likely to occur after partial gastrectomy than after any other operation—less so, perhaps, than after cholecystectomy. It may take the easily recognizable form of one or more veins in the calf muscles being affected and presenting as pain and tenderness, with mild oedema of ankle and foot. The latter may be so slight that it can only be recognized by comparing both feet and observing that the extensor tendons are somewhat masked on the affected side. Homans' sign is sometimes present, and there is usually mild pyrexia. The patient should be confined to bed, and since it usually develops on about the fifth or sixth post-operative day, it is safe and helpful to use anticoagulants. Firm crêpe bandaging is useful and it is wise to keep the patient in bed until the temperature is normal. It has been suggested that this kind of thrombosis is initiated by pressure of the calf muscles on the table during long operations, and that the risk can be minimized by putting a pad under each tendo Achilles in order to raise the legs and thus prevent continued compression of the veins within the muscles (Bailey and Love, 1959). Unfortunately, there is a more silent and treacherous form of venous thrombosis giving no warning signs whatever, the affected veins being deep femoral or pelvic, within which lies a delicately attached clot which may break off at any moment to form a fatal pulmonary embolus.

In the patient who gives a history of previous trouble with phlebitis the question of giving anticoagulants either before or soon after operation has to be considered. There is a great deal of difference of opinion concerning this because of the fear of haemorrhage from the anastomotic region and suture line. In order to be effective, prothrombin time should be reduced to 30 per cent of normal but not below. Probably the best policy in such a patient is to give phenindione after the first 48 hours following operation but, at the same time, to apply from the time of admission to hospital all the anti-stasis devices available. Should secondary or spontaneous haemorrhage occur while the patient is on phenindione the antidote is vitamin K, given intravenously.

Phlebothrombosis is one of the conditions that causes continued unexplained post-operative pyrexia, the others, of course, being wound sepsis, pulmonary or renal tract infection.

Dehiscence

If by dehiscence one means a real burst abdomen, the wound coming apart from end-to-end or at least a substantial part of it, then it is admittedly uncommon but, unfortunately, lesser degrees of breakdown are all too frequent. Even these vary, some being superficial, perhaps 2–5 cm in length, and usually the result of the collection and discharge of a mildly infected haematoma; others are deep, resulting from the strain of coughing or vomiting. The patient may sense that something 'has given way', and herniation of omentum or small intestine may result; when skin stitches are removed later there may be a full thickness breakdown of the whole wound. Inspection of the wound when dehiscence is impending reveals localized fullness, oedema or inflammatory reaction, and temperature and pulse may be raised. Such a swelling usually means a haematoma that has become infected, and the removal of one or two stitches will allow it to discharge; the infecting organism should always be ascertained. If the collection is deep to the rectus muscle it may take several days before pointing. At the same time, by contiguity with the peritoneum, it may produce irritation and peritonism, with consequent disturbance of peristalsis causing discomfort, distension, loss of appetite, possibly nausea and a delay in bowel action. When the skin stitches are removed this latter type of wound infection may be followed by a breakdown of the wound down to the peritoneum. The average surgeon will declare that dehiscence rarely occurs, yet if the above variations are accepted as dehiscence, the incidence at any hospital is unflatteringly common. My colleague, D. M. Morrissey, investigated the problem in the Queen Elizabeth Hospital between 1946 and 1952 and found that the incidence of all forms of dehiscence in 7,698 abdominal operations was 119 (1·5 per cent).

During the past fifteen years there have been changing fashions in incisions of approach, including right and left paramedian, midline, transverse and oblique in line with the left or right eighth or ninth rib. With the popularity of vagotomy, some surgeons extend the left paramedian incision up to alongside the zyphisternum, while some use an upwardly curved transverse incision. All vertical incisions involve fascial planes that are put under tension by breathing, coughing, moving in bed or by distension. These fascial planes must be approximated with the greatest care and precision; it is very easy to miss one edge, mistaking fat for peritoneum, especially in the region of the falciform ligament. Chromic catgut, thread, silk, wire and man-made fibres are all satisfactory, and interrupted sutures are better than a continuous one, especially for the upper part, where the fascial planes are held more taut by the rib cage. Should the patient be obese, the victim of chronic bronchitis or elderly, or should the operation be one concerning which experience shows that ileus is a likely complication as, for example, after the separation of massive vascular adhesions, tension sutures passing through all layers of the abdominal wall should be employed. Dead space should be obliterated wherever possible, this applying especially to the superficial layers where oozing may lead to haematoma formation. In gastric surgery there is also the factor of contamination of the wound by stomach and jejunal contents. The organisms in gastric or jejunal juice are usually scanty and often non-pathogenic, but where there has been gastric retention or where the operation is for a post-gastrectomy complication, an element of blind loop being present (the afferent loop), the bacterial content is different and may be harmful. In addition, the chemical constituents of the juices may interfere with normal healing processes, and for these reasons it is important to protect the wound edges by swabs, soaked in an antiseptic such as 1/1000 acriflavine, before opening the gut. Although no figures are available, I am satisfied that since applying this protection I have seen less wound sepsis than hitherto.

Other factors that may be associated with dehiscence in victims of peptic ulcer are vitamin C deficiency and hypoproteinaemia, although the latter is rare in this country.

The tensile strength of a wound depends on the formation of collagen in the ground substance. It does not appear until about the fifth day and results from the interaction of pro-collagen, which is produced by fibroblasts, and ascorbic acid. Any deficiency in ascorbic acid therefore interferes with healing.

A protein-deficient diet needs to be extreme before leading to hypoproteinaemia but, unfortunately, this does apply in some tropical countries. Even so, hypoproteinaemia has to be severe before interfering with healing. It results not only in lack of certain essential proteins for the healing process, but also in oedema.

When dealing with a dehiscence in which continuous suturing has been employed, fragmented catgut is often found, suggesting faulty materials; sometimes, on the other hand, the catgut may be intact, indicating that it has pulled out between parallel fibres of the rectus sheaths or of the linea alba. On rare occasions the catgut would seem to have disappeared completely, and I know of three such cases in my own hospital. This also suggests some defect in the catgut, but some reaction by the body must play a part. Nevertheless, faulty technique is the most common single factor responsible. When treating a case of dehiscence one is always impressed by how inert-looking the wound surfaces appear, as if no vital process towards healing had been going on, yet healing after re-suture is almost invariably prompt and secure. This appearance was once referred to as the 'lag phase' but, as Dunphy and Udupa (1955) point out, this is in fact a very active period, and the time of preparation for the production of collagen. Sound apposition will obviously help the healing process during this activity.

POST-OPERATIVE COMPLICATIONS ASSOCIATED PARTICULARLY WITH PARTIAL GASTRECTOMY

Haemorrhage

Reactionary—One of the minor advantages of employing gastric suction is that it reveals any reactionary bleeding which may occur from the suture line. The first few hourly specimens will almost certainly contain a little blood, but this rapidly becomes less and of darker colour in each subsequent aspirate. Unless it remains or becomes bright red, is aspirated or vomited in unusual quantities, continues for 4–5 days or is associated with a rising pulse, it is unnecessary to interfere surgically; such bleeding is rare and I have known of only three cases requiring second operation, one of which was long ago during my resident days. In most cases, reactionary bleeding responds to simple measures, such as sucking a piece of ice, and omnopon (10 mg q.q.h.) or sometimes adrenalin (1/1,000) and Stypvan (1/1,000) via the gastric tube. Should these fail, the abdomen must be re-opened and the anastomosis examined. This is best achieved by opening the stomach proximal to the stoma and inspecting the suture line from within, when an oozing area or a spurting vessel may be found. A few extra sutures will control the situation satisfactorily.

Incidental—Bleeding during the first few days after operation may arise from other causes, such as oesophageal ulceration in association with a coincident pre-operative oesophagitis resulting from reflux. Unsuspected blood dyscrasias may also account for these haemorrhages, and McLaughlin and Coe (1954) published seven cases which appeared to be associated with thrombocytopaenia. Such incidental haemorrhages occur later than the reactionary type which, of course, is the result of inadequate haemostasis. Incidentally, matters such as taking aspirin or aspirin-containing mixtures, or taking one of the cortisone drugs for rheumatism, should be enquired into; I have seen bleeding from all these causes. A late colleague of mine having had the experience of a number of patients with benign prostatic enlargement who were also known sufferers of peptic ulcer developing severe haematemesis or melaena within a day or so of prostatectomy, used to advocate operation for the peptic ulcer first. The mechanism of this intestinal bleeding after prostatectomy is unknown, yet it was perhaps not without significance that some of these patients had been given aspirin-containing mixtures for mild post-operative discomfort. Rains, Dawson-Edwards and Brookes (1957), on the other hand, published similar incidents of bleeding from a peptic ulcer following other operations, such as abdomino-perineal excision of the rectum for carcinoma. What is the connection between the incident of a major operation and the breakdown of a pre-existing ulcer of stomach or duodenum?

Secondary—Littler (1957) reported three cases of severe haemorrhage occurring 10–12 days after partial gastrectomy which, he believed, resulted from sepsis in and around the suture line, with sub-mucosal abscesses and erosion of blood vessels. All three developed pyrexia, pain, tenderness and repeated haematemeses, and one developed a palpable mass. All were treated with antibiotics and sulphonamides and the case with the mass was drained; all recovered. Littler's suggestion that this combination of events forms a definite syndrome seems justified and, even in the absence of haemorrhage one meets, from time to time, a patient with prolonged or more marked post-operative pyrexia than usual, associated with discomfort and tenderness, yet with none of the common causes of continued temperature.

The following case was an instance of delayed haemorrhage, probably the result of erosion, presenting itself in a curious way.

C. C., aged 54, had suffered dyspepsia for twenty years. In 1937 gastro-enterostomy was performed at another hospital, but without complete relief. In 1948 partial gastrectomy was carried out at the same hospital, again without full relief. In 1956 he was admitted to the Queen Elizabeth Hospital, Birmingham, having suffered during the previous nine months from worsening attacks of severe pain and vomiting of much bile, unrelieved by medical treatment. The pain came on 2 3 hours after meals and radiated into the right shoulder. It was relieved by vomiting but sometimes caused fainting. He had also suffered from diarrhoea for the past 12 months.

The general pattern of discomfort, combined with the vomiting and diarrhoea, suggested that the afferent loop had become embarrassed by adhesions.

An operation on 27th September 1956, proved the gastrectomy to have been of the ante-colic type with afferent loop 30–40 cm long. This had become concertina'd and tethered in such a way that obstruction could be produced when the loop became full. There was no evidence of stomal ulcer. The anastomosis was taken down and the jejunum reconstructed. A new ante-colic anastomosis was effected within 10 cm of the duodeno-jejunal junction, the retro-anastomotic gap being closed. Progress was satisfactory until the eleventh post-operative day, when he was seized with severe pain and showed signs of internal haemorrhage. On re-opening the abdomen that day the stomach reservoir was found to be grossly distended. It was opened through an anterior incision and two pints of clot were evacuated. No ulcer or bleeding point was found. A second incision was therefore made into the efferent loop but, again, no bleeding point was discovered. From this complication he recovered satisfactorily, and at the first review had gained weight. The source of haemorrhage is difficult to say, but it might have been a small erosion on some part of the anastomotic line, or it could have been an example of the Mallory Weiss syndrome.

Stomal Dysfunction

Assuming that the post-operative régime outlined above has been followed, one would not expect hourly aspirates from the second day onwards to exceed that given by mouth, any excess over intake being a mixture of gastric secretion, swallowed saliva, old blood and lymph; occasionally, however, they amount to much more, totalling as much as 1 l. or more in 24 hours, indicating retention.

Stomal Oedema; Stomal Fibrosis; Mechanical Fault at Stoma—Oedema of suture line is more common following the Billroth I operation than gastro-jejunostomy, especially when a direct end-to-end, rather than end-to-side, gastro-duodenostomy has been employed. So long as fluid and electrolyte balance is maintained by parenteral means, it is safe to await events, since the aspirates usually fall to 20–50 ml/h by about the third or fourth day, indicating a clear way through the stoma. Most cases of difficulty result from temporary oedema, but occasionally some unexplained feature or some fault in technique is responsible. After 10–12 days I should feel bound to re-open the abdomen, even though the patient's nutritional state were satisfactory; I have had to do this in two patients. In the first case, the anastomotic ring had become stenosed and fibrotic even at this early date, and had to be excised. The reason for this narrowing was not clear even after histological examination; an exactly similar case was encountered by another member of the Unit. In my second case, a Pauchet pattern of Billroth I operation had been performed, and an over-wide stomach at the anastomosis had formed a small diverticulum at its lesser curve junction with duodenum which, when filled with food, blocked the stomach; this diverticulum had to be removed.

Detachment of Meso-colon from Stomach; Torsion of Afferent and Efferent Loops—With the retro-colic type of reconstruction, gastric outflow may be hindered by the simple occurrence of the stitches attaching the edges of the meso-colon to the stomach stump pulling out so that the meso-colon slips downwards, pulling together afferent and efferent loops. On the other hand, retention may also result from partial torsion of the efferent and afferent loops on the axis of the anastomosis leading to embarrassment of the stoma, sometimes amounting to near-obstruction. This complication is almost confined to retro-colic operations.

If gastric retention persists for longer than 4–5 days, x-ray studies of a thin barium meal should be made, and if these confirm that little or nothing passes through the stoma, a further operation is called for. On inspecting the anastomosis—nearly always of the retro-colic type as already stated—it is found that whereas at the end of the initial operation the afferent and efferent loops appeared to lie side-by-side, they have now become rotated in such a way that the efferent loop lies in front hiding the afferent loop or, very occasionally, the other way round, thus producing a twist which interferes with the smooth passage of gastric contents into the jejunum.

The following case is an example of both slipping meso-colon and torsion of the anastomosis.

J. F., a man of 45, suffering from the dyspepsia of duodenal ulcer, was referred to me by a medical colleague because of recurrent activity of his ulcer. A retro-colic Billroth II partial gastrectomy was carried out and the usual post-operative treatment given. Suction volumes remained high and on the fourth day he began to vomit too. A small barium meal showed that little was passing through the stoma and the radiologist suggested that the stomach had retracted upwards with consequent approximation of afferent and efferent loops, probably the result of the meso-colon having become detached. The abdomen was re-opened; the efferent loop lay in front, having swung over to the right and had become pressed into this position by the weight of the meso-colon and fixed thus by adhesions (*Figure 2*). The stitches between the edges of the meso-colon and stomach had torn out, as suggested, thus allowing the meso-colon to slide downwards. In this case, I separated the adhesions and re-sutured the transverse meso-colon to the stomach in such a manner that the efferent loop lay on the left of the afferent. This patient has remained satisfactory for six years. It so happens that although the operation was a retro-colic

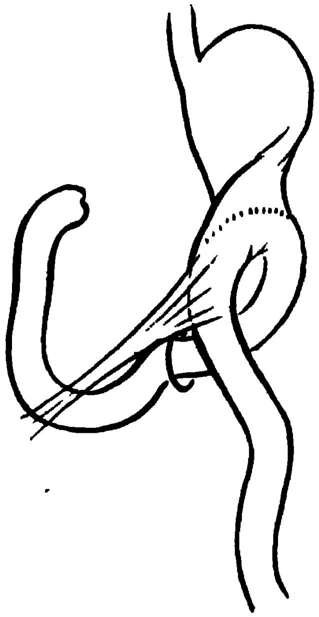

Figure 2. Rotation of loops. Efferent loop lies in front of afferent. A peritoneal band is partly responsible

one, I had made the afferent loop some 10 cm long; this, of course, was a mistake—there should be no afferent loop at all—and this long loop may have been partly responsible for the rotation by insinuating itself under the upper mesentery and pushing it to the left, thus impinging on the afferent loop.

A second case is another example of this rotation of loops.

In January 1956 W. A. R., aged 46, was admitted to the Medical Unit having suffered six episodes of melaena since 1951. In 1954 a barium meal elsewhere showed a duodenal ulcer but laparotomy at the same hospital failed to confirm this or to reveal any other source of bleeding. Further melaenas occurred and he was admitted to the Queen Elizabeth Hospital. At laparotomy a large posterior and a small anterior duodenal ulcer were found. A three-fifths retro-colic partial gastrectomy was performed, afferent loop to lesser curve, again the loop being 10 cm long. The meso-colic edges were stitched to the stomach. The Ryle's tube was removed on the third day, but on the sixth day vomiting developed. The Ryle's tube was replaced and aspirates remained large, suggesting stomal obstruction. A small barium meal confirmed that very little passed out of the stomach. On the tenth post-operative day he was re-opened and the anastomosis was found to have undergone rotation, the efferent loop being in front and lying to the right and firmly adherent to the under surface of the meso-colon, the edges of the latter having become detached from the stomach stump, as in the previous case. In this case entero-enterostomy was carried out. Recovery was satisfactory and when seen in February 1962 he said that 'he had had a few episodes of discomfort, but no more bleeding, and was really very well indeed'. Today I would have added vagotomy and realize that we have been lucky that no stomal ulcer has developed. It is true that the 10 cm afferent loop made the entero-enterostomy possible; nevertheless, it is repeated, there should be no 'afferent loop' in a retro-colic operation.

There are certain points of anatomy concerning the duodeno-ejunal (D.J.) junction that are of importance to the surgeon; this unction lies to the left of the midline. A careful study of the junction eveals certain folds of peritoneum associated with the uppermost art of the jejunal mesentery, which vary in different patients and vhich determine the lie of the first few centimetres of the jejunum; ometimes forward and to the left, sometimes directly forward, ometimes forward and to the right. Often, these can only be seen n the living patient. Dr G. Bentley, of the Department of Anatomy n Birmingham, has very kindly investigated for me this region in odies from the dissecting room and post-mortem department, and n 30 specimens has found only a suggestion of these folds in one pecimen. For the last 18 months I have examined the D.J. junction in every abdominal operation I have performed, and have found the arrangements now to be described on at least twenty occasions. If one recalls the pictures in anatomy textbooks of the peritoneal arrangements on the posterior abdominal wall, the attachment of the mesentery is usually portrayed as in *Figure 3(a)*. However, when studied in the living patient during operation one sees that its form may, instead, be as in *Figure 3(b)* or *(c)*, and that with this latter arrangement the uppermost part of the jejunum is directed to the right. With this arrangement there is often also a fold of peritoneum between this part of the jejunum and the peritoneum covering the pancreas at about the midline, which tends to hold the jejunum over to the right. My colleagues of the x-ray department assure me that evidence of this arrangement can be seen by radiography. In addition to this fold there is sometimes yet another between it and the under surface of the right half of the meso-colon; this was described by Moynihan (1928).

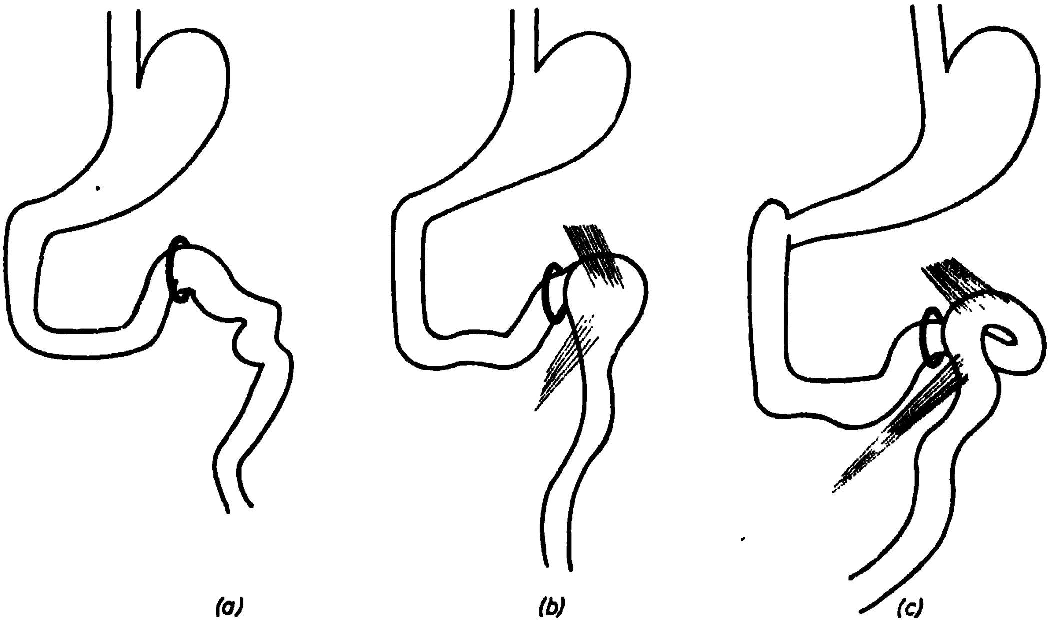

Figure 3. Different arrangements of origin of the mesenterae and its effect on the duodeno-jejunal junction

There seems little doubt that these anatomical features are responsible for the rotation or torsion that sometimes occurs within the first few days following a retro-colic Billroth II operation. It is important to respect these anatomical arrangements and to attach the jejunum to the stomach in such a manner that it lies absolutely naturally. Thus, if the upper jejunum passes forward and to the right, a fairly common pattern, it should be attached to the stomach in this line; otherwise, a short afferent-loop-to-lesser-curve anastomosis would produce a twist. With such a formation, the Moynihan type of reconstruction is the correct one, i.e. afferent loop to greater curve. Once again, it is stressed that the term 'afferent loop' refers only to small intestine caudal to the duodeno-jejunal junction, and that in the retro-colic operation the anastomosis should abut on to the D.J. junction. An alternative solution is to cut these folds so that the efferent loop will not tend to roll over to the right. Taylor (1959) goes even further and mobilizes the junction including division of the ligament of Treitz, thus leaving no afferent loop at all.

In both the cases recorded above, two factors were present, namely, the downward slipping of the meso-colon and the rotation of the afferent and efferent loops. Either would interfere with gastric emptying, the torsion by distorting the stoma, and slipping of the meso-colon by crowding the region of the anastomosis and approximating both loops. In both cases the twist remained even after adhesions between the meso-colon and anastomosis had been separated. On testing the effect of raising or lowering the freed meso-colon, it was observed that when it was allowed to slip down again it accentuated the tendency of the loops to rotate, presumably as a result of pressing the anastomotic region backward against the posterior abdominal wall. All things considered, I feel sure that in these cases the torsion was the primary cause of obstruction, and that the detached meso-colon was incidental.

When faced with such a problem, therefore, it is the torsion that must be treated. At this stage, i.e. 3–6 days after the first operation, there will be not only sticky adhesions but also thickening of responsible folds of the peritoneum, and cutting the folds will now be ineffective in reducing the twist. Entero-enterostomy between the two loops will be difficult to perform unless the afferent loop is longer than normal. Personally, I now advocate conversion to a Billroth I operation combined with vagotomy.

Similar mechanical factors are, of course, associated with simple gastro-enterostomy; it is interesting to note that, for this operation, Moynihan imposed strict rules calculated to prevent any such twist or torsion as recounted above, although, in fact, only if the lie of the upper jejunum is forward and to the right will the method he described prove satisfactory.

The incidence of this complication of torsion is low, yet most surgeons who have performed several hundred partial gastrectomies will admit to having encountered two or three such cases.

Clot Bezoa of Stomach—A somewhat rare cause of stomal obstruction was found in the following case.

W. P., aged 58, had suffered for nine years from dyspepsia of duodenal ulcer type with several incidents suggesting penetration. X-ray investigations were negative on repeated occasions. He was admitted to the Queen Elizabeth Hospital in 1947 when laparotomy revealed an anterior duodenal ulcer. Retro-colic gastro-enterostomy was carried out (today, of course, vagotomy would have been added). He remained well for 12 years, and then developed abdominal pain and had lost weight. There was no vomiting. Full investigations were carried out, and the only positive finding was delayed emptying of stomach, but no evidence of ulcer.

At laparotomy in November 1960 a large ulcer was found on the posterior rim of the stoma penetrating into the pancreas. There was also marked stenosis of the second part of the duodenum. Two-thirds of the stomach, including the area of the stomal ulceration, was excised and reconstruction was by ante-colic Billroth II technique. After a stormy post-operative course it was difficult to persuade him to take food, and during the next two months in spite of high caloric diet he lost weight and continued in a vaguely unsatisfactory state and vomiting occurred from time to time. A barium meal was therefore x-rayed which showed what appeared to be a bezoa in the stomach (*Figure 4*). On 9th January 1961, a further laparotomy was performed and on freeing the stomach from adhesions, a firm mass could be felt within. The stoma itself was of satisfactory size. The stomach was therefore opened and the bezoa removed. It was found to be firm and cheesy and consisted mainly of clotted milk, the whole weighing 300 g. The stomach was sutured and the abdomen closed. From this time onwards he made satisfactory progress and in February 1962 was well.

Meso-colic or Omental Fat Reaction Affecting the Stoma—Very rarely and, indeed, fortunately so, the fat in the omentum or meso-colon appears to undergo a violent reaction whereby it becomes immensely thickened—up to 2–3 cm—and adherent to everything in the vicinity. In a retro-colic gastro-jejunostomy the thickened adhesive meso-colon gains a rigid stranglehold on the stomal region and causes obstruction. In an ante-colic anastomosis the greater omentum, undergoing a similar fibrotic reaction, may become plastered around the anastomosis and again may cause obstruction. It may be difficult to determine the cause of the reaction. Kirschner and Garlock (1954) refer to 'sterile inflammation' or 'necrosis' and suggest that it is the result of interference with the blood supply of either meso-colon or omentum. This interference is particularly likely in the omentum, the blood supply of which lies entirely in the anterior two layers. They thought that patients undergoing gastrectomy for cancer, in which the whole omentum was removed, ran a smoother course than those following operation for ulcer, where the omentum is preserved, and they advocated routine

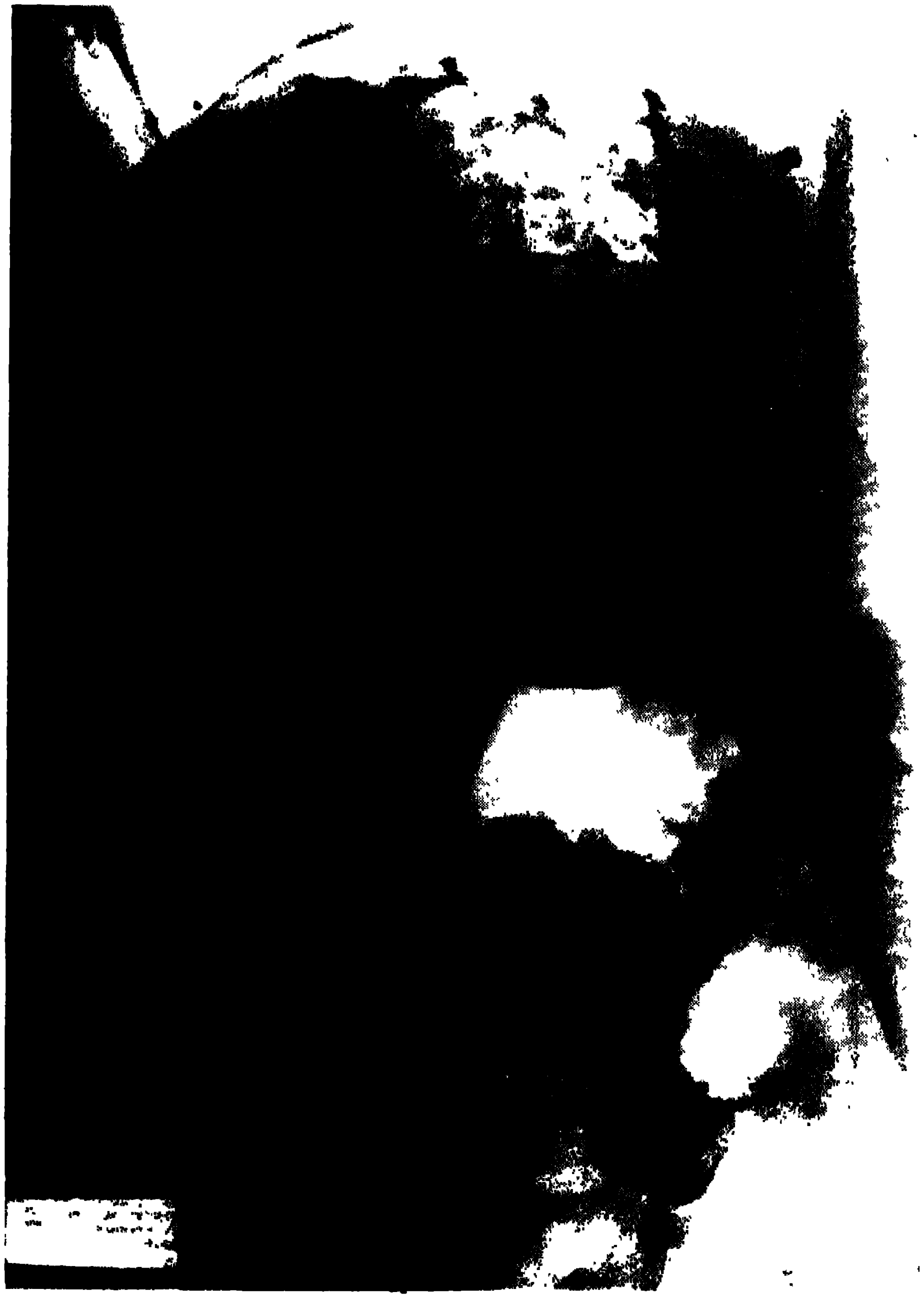

Figure 4. Clot bezoa

omentectomy. A similar reaction, with great thickening, resulted from ligation of the omental vessels in experimental animals. With regard to this observation, one wonders whether the mass ligation of large parts of the omentum which some surgeons employ during preparation for partial gastrectomy may not increase the risk of injury to major blood vessels. Others have argued that this reaction is due to a minor leak in the suture line, to which the omentum has become adherent with consequent inflammatory reaction. This hypothesis, too, is supported by work in experimental animals.

The clinical manifestations of this complication of fat reaction are the symptoms of embarrassment at the stoma persisting beyond the fifth post-operative day. If x-ray studies confirm a rigid stomal narrowing a second operation may be indicated. I have encountered two such cases in which the omentum was affected and can confirm the finding of a most difficult situation at operation. In both, an immensely thickened omentum, feeling almost like gristle, was stuck firmly to the anastomosis. Its separation required considerable dissection and resulted in much troublesome oozing. I feel that the hard tissue must be excised, otherwise the strangling process will be repeated. Should it be the meso-colon that is involved, the difficulties are even greater since the anastomosis is more difficult of access, and the blood vessels endangered in the dissection include the middle colic. It is therefore best, in this situation, to take down the anastomosis and to convert either to an ante-colic Billroth II, or to a Billroth I reconstruction plus vagotomy since, if one does not, the fiercely adhesive reaction may recur, and the whole obstructive process be repeated.

I know no device for preventing this phenomenon. Care with the suture lines, respect for blood supply and restraint from ligaturing too large sections of anterior layers of omentum seem the only safeguards. My own two cases are as follows:

L. R., aged 34, had a long history of indigestion. In 1949 a barium meal revealed a duodenal ulcer. Attacks of typical duodenal ulcer pain recurred during the next ten years. The attacks became worse and by July 1960 were complicated by occasional vomiting, and a loss of 14 lb. in weight. On 4th August 1960, a retro-colic Billroth II three-fifths gastrectomy was performed. It was noted at the time that the upper 15 cm of the jejunum was adherent to the under surface of the meso-colon, and it was necessary to separate this early in the operation. On the sixth and seventh post-operative days he vomited a little bile, but this cleared up and he returned home on the ninth day. Two days later he was re-admitted fairly severely dehydrated, having vomited almost continuously for the previous 24 hours, each vomit consisting of heavily bile-stained fluid. Nothing abnormal could be felt in the abdomen but bowel sounds were absent. Parenteral fluid and electrolyte replenishment was established, and during the next 24 hours gastric suction produced 3 l. of bile-stained fluid. All these features suggested obstruction of the efferent loop. On 16th August 1960, the abdomen was re-opened. The omentum had undergone some process which was interpreted as inflammatory or ischaemic reaction. It was about 2·5 cm thick and firmly adherent to the meso-colon, the two together having a veritable stranglehold on the retro-colic anastomosis and affecting the efferent loop more than the afferent. It was impossible to identify the stoma through the thickened tissues. There was no dilatation of the duodenal stump. The thickened omentum was separated from the meso-colon but this process was especially difficult where its edge surrounded the anastomotic area. There was no evidence whatever of any leak and no visible abscess within the separated omentum or mesentery. Because there seemed a risk of recurrence it was decided to convert the retro-colic anastomosis to an ante-colic one, and the omentum was excised.

Progress was slow at first, but after 13 days he rapidly improved. When seen in April 1962 he was completely free from all pain or dyspepsia.

An example of this omental reaction in association with a leak in the anastomotic line is the following:

In 1951, V. D., a man aged 52, had been treated elsewhere for duodenal ulcer by an ante-colic Billroth II, 70 per cent gastrectomy, afferent loop to lesser curve. He remained well until 1955, when he was admitted under my care in a collapsed state suffering from melaena. There was no pain or vomiting and he responded well to blood transfusion. Barium meal studies showed the mucous membrane in the region of the stoma to be coarsened, but no stomal ulcer was revealed. Gastroscopy revealed a very small gastric reservoir, but there was again no sign of ulcer. He was then discharged, but between August 1956 and July 1957 he suffered several further melaenas, and operation was therefore advised. On opening the abdomen adhesions from the first operation were so widespread that initially it was difficult to find the coelomic cavity. The gastrectomy was found to be a high ante-colic Billroth II type, and the afferent loop was about 25 cm in length. No stomal ulcer was recognizable until the anterior part of the stoma was opened, when a healed ulcer with a typical white fibrous base was seen on the efferent loop side. A vagotomy was carried out and the Billroth II gastrectomy converted to a Billroth I reconstruction, the opened part of the jejunum being excised and end-to-end anastomosis being effected. After operation his general condition was good but gastric aspirations continued to be excessive and he did not have a bowel action until the tenth post-operative day. On the twelfth day a fistula developed in the upper end of the wound discharging up to 1,500 ml of bile and gastric contents. Attempts were made to control this by re-establishing gastric suction and applying suction to the superficial part of the fistula, without success. The x-ray of a barium swallow is shown in *Figure 5.* On the 21st post-operative day, therefore, it was decided to re-open the abdomen. Extensive adhesions had re-formed and were very thick, tough and vascular, and the region of the anastomosis was stuck firmly to the under surface of the liver. The omentum, which was intensely oedematous, had wrapped itself round the transverse colon and was adherent to the anastomosis above, and to the region of the duodeno-jejunal junction below. Gradually, the upper jejunum was freed by almost

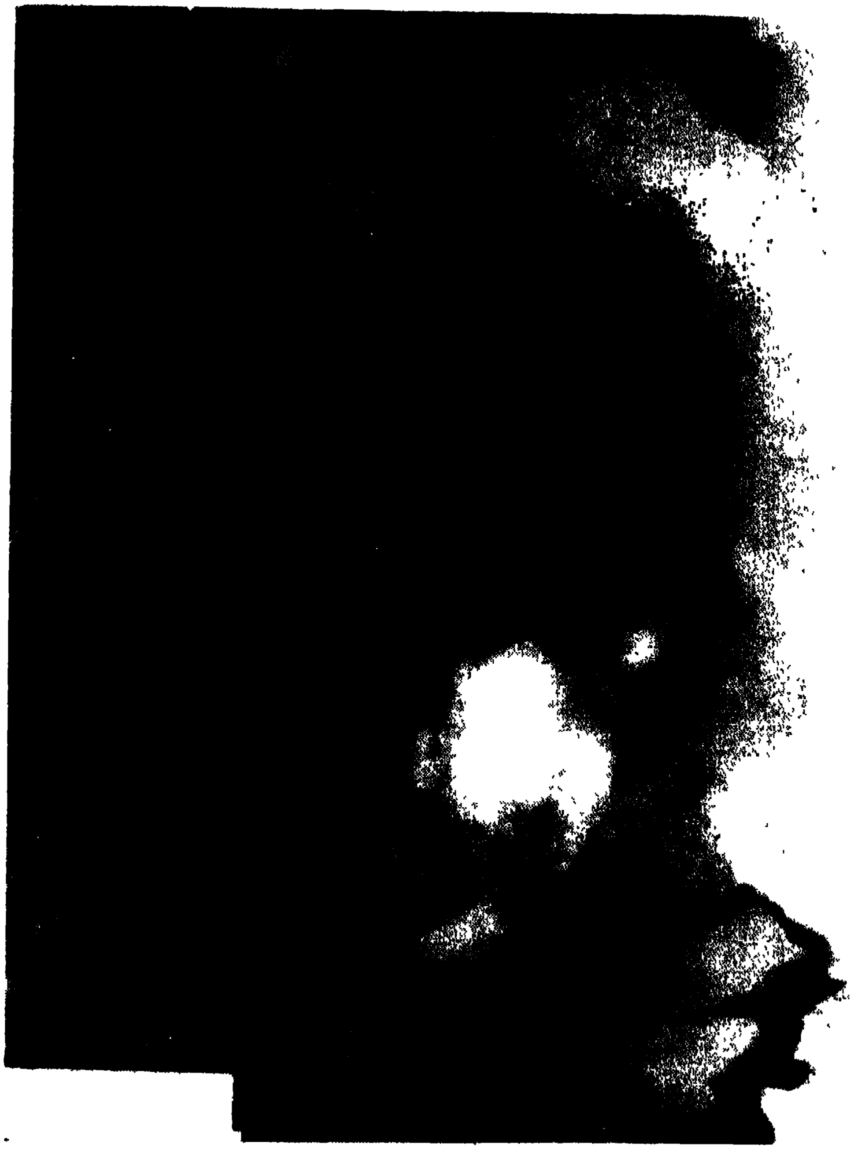

Figure 5. Gastro-duodenostomy enveloped and narrowed by greatly thickened omentum

forceful blunt dissection or frank incision. At first, no fistula could be identified in the gastro-duodenostomy line, so methylene blue was injected down the gastric tube and almost immediately appeared from the back of the anastomosis. It was impossible to gain access to this fistula because of general thickening and oedema so a feeding jejunostomy was created and the abdomen was closed. Naso-gastric suction was continued.

Convalescence was protracted but he was discharged at the end of six weeks with a good appetite and with the wound having completely healed. There seems no doubt that, in this case, the anastomotic leak was the cause of the omental reaction.

When last seen in February 1962 he described himself as 'very much alive and well', and that he had been so ever since the 1957 operation.

Duodenal Rupture or Leak

Acute—With growing personal experience this becomes a less common complication than ten years previously and I have not encountered one for over ten years. Nevertheless it still occurs. Sometimes the whole suture line seems to break down suddenly, often on about the third day, with resulting flooding of the abdomina cavity with duodenal contents, consisting mainly, of course, of bile and pancreatic enzymes, which leads to rapid and severe hypovolaemia and hypotension. The collapse tends to be so profound that there may be a deceptive absence of abdominal rigidity, yet the only hope of rescuing the patient from this lethal state is to re-operate and stop the continued leak by suture and drainage. I diagnosed early, prompt treatment of the collapsed state by intravenous blood, plasma and electrolytes, together with noradrenalin and cortisone, may make operation possible.

From time to time, however, a smaller part of the suture line gives way, with a more gradual leak, and then the signs and symptoms give sufficient warning for exploration to be undertaken with the patient still in reasonably good condition.

During a visit to Canada and U.S.A. in 1950, I was told that in many centres this incident was, at that time, responsible for 50 per cent of operative mortality. The general belief was that healing was impaired as the result of damage to the blood supply during the dissection of the first part of duodenum from the head of the pancreas, particularly when it contained a posterior penetrating ulcer. Digestion of absorbable sutures was also thought to contribute to the disaster.

A number of cases of leaking stump have been reported where the afferent loop has been found distended, suggesting that it had become obstructed soon after the original operation; the most likely cause for such obstruction is rotation or torsion around the gastro-jejunostomy as already described under 'stomal dysfunction'. There is no doubt in my own mind that obstruction plays a major part in rupture or leak of the duodenal stump. At the same time, however, any weakness in the suture line itself adds to the risk.

Prevention—Every surgeon today should be alert to the danger of stump leakage and should take meticulous care in closing the stump as well as in preventing stomal embarrassment. Most surgeons employ three layers of sutures and some also cover the stump with any tags of fat or peritoneum that may be available. As already stressed, avoidance of any twist or kink at the anastomotic line is fundamental.

Treatment—In the event of a leak the stump must, of course, be repaired and, where any afferent loop obstruction is found, this must also be corrected in one of the ways already suggested, depending on the general condition of the patient. For instance if, despite careful preparation for the second operation, a re-fashioning of the gastro-jejunostomy would appear to be too time-consuming for safety, an entero-enterostomy will drain the blind duodenal loop; ideally, of course, vagotomy, if not already carried out, should be added in order to eliminate the neurogenic stimulus to acid secretion and so reduce the risk of stomal ulceration at the new anastomosis. However, the patient may not be fit for this refinement, certainly if elderly and bronchitic.

Duodenal Fistula

Occasionally the leak from the duodenal stump is so gradual that adhesions develop and localize it temporarily; then, after a period of suspicion of a developing abscess in the right hypochondrium, it may declare itself as a fistula. If the defect in the duodenum is sufficiently wide to lead to external loss of most of the bile and pancreatic enzymes, this interferes with the breakdown of proteins and fats in food which, after some days, leads to negative nitrogen balance and reduced caloric retention, while the loss of fluids and electrolytes results in dehydration and salt depletion. Even smaller fistulae are still a problem because of the digestive properties of the mixture of pancreatic and duodenal secretions contained in their discharge which may lead to widespread excoriation of the skin, causing the patient great pain and distress.

There are various ways of protecting the skin, the most important of which is to control the discharge by suction. If excoriation has not yet occurred, a plastic adhesive or 'Baltimore' aluminium paste will protect the skin; if excoriation has already taken place, gauze or lint soaked in dilute skimmed milk is helpful since, by its protein, sugar and fat content, it uses up the enzymes, abolishes pain and allows of healing. I find that the application of milk powder is also effective. Others have suggested plugging the fistulous track with a paste of oatmeal or of a mixture of egg yolk and kaolin. According to Chambler (1958), posture can also help considerably, the more nearly upright the patient is nursed, the better; this would be varied by changes to lying on the left side in order to encourage the onward flow of bile and pancreatic juices through the duodenum. Suction of the track is best achieved through a tube by a mechanical pump, and the fluid and the urine should be measured and analysed for electrolyte content in order to guide one in replacement therapy. Care should be taken that the tube is passed only about 2·5 cm down the track, for if it is pushed in too far it may then enter the lumen of the stump, thus preventing closure by healing. Should the discharge become excessive, i.e. more than 1 l./day, it strongly suggests an obstructive factor, such as rotation at the gastro-jejunostomy. Duodenal fistula usually develops after stomal oedema has already subsided, so that it is rarely worth temporizing with gastric suction in the hope that oedema will subside. The potentialities of fistula are serious, and malnutrition may become marked quite rapidly. For this reason, some surgeons at this stage advise a jejunostomy for feeding purposes, and the feeds should include the fluid aspirated from the fistula. With the more satisfactory products now available for parenteral feeding, such as fat emulsions, of which 'liponisel' and 'intra-lipid' are examples, and protein hydrolysates, such as 'aminosol', up to 2,000 calories can be given every 24 hours by the intravenous route; by a feeding jejunostomy, more than double this quantity can be given.

Abscess Formation

The leak may be so gradual that a local abscess develops in the right sub-hepatic region, gradually declaring itself by localized pain and increasing tenderness, pyrexia and rising pulse. Even more rarely the pus tracks into various parts of the abdomen in a most bizarre fashion. I had one patient who became vaguely unsatisfactory after operation, with raised temperature and pulse, and slight distension and discomfort in the left hypochondrium. There was no collapse of lung, although the x-rays revealed a raised left diaphragm and a small quantity of air lay under it. A diagnosis of the left sub-phrenic abscess was made. Exploration through a left sub-costal incision was made, and presence of the abscess was confirmed, but it was found to have tracked from right to left from a leaking duodenal stump (*Figure 6*).

Leaking Anastomosis

Like duodenal leak, breakdown of the main anastomosis is becoming less common, but still occurs. From time to time, for instance, the upper end of the abdominal incision becomes inflamed an within a day or so fluid oozes from between stitches. If this flui resembles neither pus nor blood-stained serum, the question of leak from the anastomotic line is considered. The discharge ma look suspiciously like milk; on one occasion, a patient who ha

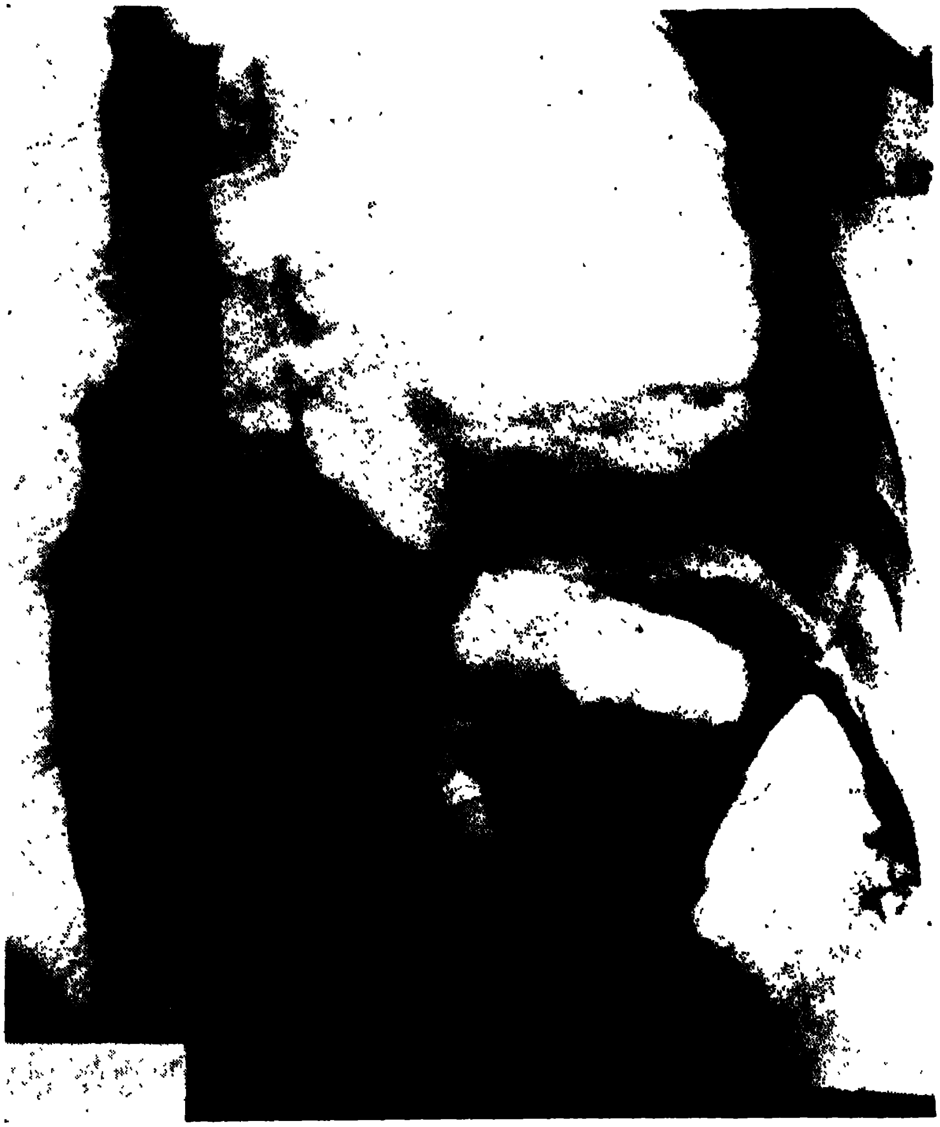

Figure 6. Left sub-phrenic abscess due to a leaking duodenal stump

reached the stage of semi-solid food complained, after a meal, o increased discomfort in his already uncomfortable wound. In hi dressing was found a considerable portion of his recently taken eg omelette. Despite this, re-establishment of gastric suction and intra venous drip for two days resulted in the wound healing soundl and definitively. The development of the leak is usually slow (there is no obstructive factor as may be the case with duodenal leak), and the area is well shut-off from the general abdominal cavity by adhesions so that it may take the form of an abscess between the anastomosis and the anterior abdominal wall. If in doubt, something easily recognizable, such as methylene blue, can be given by mouth, and will be seen oozing or running from the wound within a few moments. Treatment by gastric suction and parenteral fluids for two or three days nearly always leads to early healing. The following case represents a mixture of several of these complications.

In 1952 F. J., aged 28, was admitted to another hospital with perforated duodenal ulcer following a year's history of dyspepsia. He was treated by simple suture and recovered satisfactorily. Dyspepsia returned and in August 1954 the same surgeon performed ante-colic partial gastrectomy, but because of severe scarring of the first part of the duodenum he closed the pre-pyloric region, removing the mucous membrane of the antrum first, according to the technique of Bancroft. A few weeks later, the patient was admitted to the same hosptial, this time with pain and a palpable mass in the right hypochondrium. This was explored and thin odourless pus was found, forming a peri-duodenal collection; this was drained and healing soon took place. In early December of the same year he developed a second abscess, accompanied by pain and diarrhoea. The abscess was again drained but the discharge continued. He was then transferred to the Queen Elizabeth Hospital. He was pale and thin, and there was a vague, tender swelling to the right of the umbilicus and thin sero-pus was emerging from the drainage tube. A barium meal revealed a high Polya-type partial gastrectomy which emptied well, and there was no evidence of stomal ulcer or jejunitis. On 22nd December 1954, a right paramedian incision was made over the swelling. The posterior rectus sheath was greatly thickened, and just beneath it was an abscess of thick pus containing *E. Coli.* The cavity appeared to be shut-off from the remainder of the peritoneal cavity and an appendix abscess appeared to be the most likely diagnosis; the cavity was drained. He improved rapidly, and the wound healed.

Three months later the site of the drainage tube opened spontaneously and discharged thin fluid. A sinogram could now be performed and this showed a communication with the duodenal stump. On 21st March 1955, the abdomen was opened by a right sub-costal incision. The appendix was long and kinked, but not inflamed. A probe introduced into the sinus passed towards the duodenum. Adhesions around the gall bladder were separated and deeper down there was a swelling some 2½ in. in diameter which proved to be the region of the pylorus, with some mucous membrane still visible. This swelling was excised and the duodenum closed. The appendix was also removed. His convalescence was satisfactory and he remained well for the next six months, but then began attacks of vomiting greenish-yellow fluid after meals, this occurring most days.

In September 1956 he was admitted once again to the Queen Elizabeth Hospital because the vomiting of bile had continued, sometimes with pain. His nutritional state was only moderate. The haemoglobin was 96 per cent and fluid and electrolytes were in balance. The serum proteins were normal. Tests for occult blood were negative on three occasions. Because a barium meal showed retention of barium in a distended afferent loop, it suggested some degree of obstruction of this loop, but there was no suspicion of ulcer. At operation, massive adhesions were encountered on the right. The efferent loop was greatly distended and concertina'd by adhesions. The afferent loop was rather long, but not distended, yet the symptoms had been suggestive of afferent loop syndrome. It was therefore argued that this resulted from the distended efferent loop abutting on the stoma in juxtaposition with the afferent loop, thereby hindering free emptying. Despite separating adhesions there remained an organic kink in the efferent loop near to the stoma; this was corrected by a plastic procedure, which allowed the hitherto distended loop to collapse.

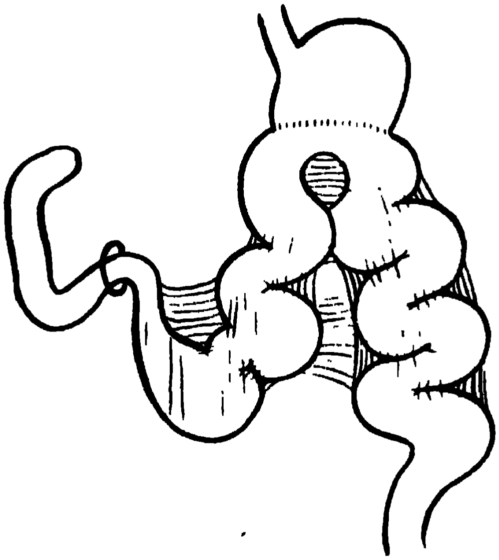

Figure 7. Concertina'd afferent and efferent loops

Unfortunately, the bilious vomiting returned soon after returning home and occurred after every meal. He was therefore re-admitted on 1st November 1956. Laparotomy again revealed massive adhesions and, on this occasion, both loops were held in a ruckled-up state (*Figure 7*). After separating the adhesions, the two loops lay side-by-side and a Steinberg pantaloon operation was carried out. He made an excellent recovery and at a series of follow-up interviews, the latest being in August 1962, has expressed himself as very well.

Pancreatitis

This is not a common complication in this country but when it does develop it is extremely dangerous, often fatal, the mortality being in the region of 70 per cent (Howard and Jordan, 1961). I have not encountered such a case for nearly ten years. Its cause is not certain, but there are many theories. It is more common after operations for duodenal ulcer than for gastric ulcer, and one realizes that injury to the head of the pancreas and its duct system may be caused during dissection of a posterior penetrating ulcer, resulting in the escape of pancreatic juice. If this were so, it is perhaps surprising that it does not happen more often although, admittedly, a penetrating ulcer usually has a fibrous base which, presumably, acts as a protective barrier. Millbourn (1949) and Dunphy, Brooks and Achroyd (1953) suggest that damage to the main blood supply to the head of the pancreas—the pancreatico-duodenal artery—may be responsible; and venous thrombosis and auto-digestion must also be included as possible aetiological factors. Warren (1951) discusses this well in reporting eight cases.

The diagnosis of post-gastrectomy pancreatitis is often very difficult. A rise in serum amylase does not necessarily prove pancreatitis, unless it is persistently in the thousands, since it can also accompany intestinal obstruction, including acute afferent loop obstruction or a leaking anastomosis. The patient becomes collapsed, often suddenly, and abdominal physical signs may be suppressed. Slaney, one of my colleagues, likens the effect of pancreatitis to a third degree burn of the peritoneum, with rapid loss of fluid and blood via the damaged area—a good analogy.

The two cases that I have encountered appeared to be satisfactory for the first 48 hours after gastrectomy and then collapsed fairly suddenly on the third day. The one case presented with sweating, pallor, hypotension, rapid pulse and a temperature of 97°F, but no abdominal signs whatever, so that one thought of a coronary occlusion or a state of salt depletion. He died despite supportive therapy but not until autopsy was the true cause revealed. This incident was in 1948, and I think that in the presence of such a collapse after gastrectomy today one would be more alert to such a possibility and forthwith befit him for further operation by restoring blood volume by blood, plasma and other fluids, together with cortisone and noradrenalin. Some centres are also giving pancreatic enzyme inhibitors. The second case presented with signs of peritonitis and was diagnosed as rupture of the duodenal stump, but when the abdomen was re-opened widespread fat necrosis and free blood-stained fluid immediately revealed the true diagnosis. The pelvis and loins were drained, and fluid and electrolyte replenishment established, but without success.

Since it has been suggested that dissection of a posterior duodenal ulcer penetrating into the head of the pancreas may be associated with subsequent development of leaking duodenal stump on the one hand, or of pancreatitis on the other, it raises the question of how best to deal with penetrating posterior ulcers. Some surgeons include the ulcer in the same stitches as are used to close the duodenal stump in a kind of 'cobbling-up' process. Others detach the ulcer from the pancreas by incising the periphery of the ulcer, thus leaving the base behind and a hole in the wall of the duodenum. This latter is connected by incision to the opening of the transected duodenum, and then the whole is sutured in layers in such a manner as to produce secure closure. Bentley (1952) discussed this problem well.

Peritonitis

This has been covered in part when dealing with leaking duodenal stump or main anastomosis, and with pancreatitis. In addition to these causes, a low grade general peritonitis may be encountered, possibly as a result of contamination by intestinal contents during operation. The suspicion of peritoneal inflammation arises because of increasing abdominal discomfort, distension, slow return of bowel sounds, or diminution after earlier return, tenderness, continued pyrexia and raised pulse, and tenderness in the pelvis on rectal examination. The outcome may be resolution, but complications such as ileus or sub-acute obstruction may develop, and death may result.

Abscess formation may develop and, when antibiotics have been used in inadequate doses, there may be multiple abscesses isolated from one another by dense fibrotic peritoneal and omental reactions. This is a dangerous condition, because the adhesions are difficult to deal with and it may not be possible to identify all the collections of pus; furthermore, multiple, scattered abscesses are always difficult to drain. It must be repeated that contamination by intestinal contents, even though of the upper part of the tract, may be dangerous when there has been stasis, and it is wise to protect the wound edges with swabs soaked in some mild antiseptic, such as 1/1,000 acriflavine before opening the stomach and jejunum.

The treatment of peritonitis is really the treatment of its complications and these are dealt with under respective headings.

Ileus

After most abdominal procedures, bowel activity is subdued—but not abolished—during the first 48 hours, and bowel sounds tend to be greatly reduced. Provided the bowels have been well prepared before operation, the absence of a bowel action for 2–3 days is not important; discomfort from wind can usually be relieved by a simple enema or suppositories. If a feeling of fullness is complained of without periodic pain and if distension develops, combined with a relatively silent abdomen, the onset of ileus must be feared. Not every cause of ileus is known but prolonged manipulation of the bowel, free blood in the peritoneal cavity following separation of adhesions, and low-grade peritonitis from contamination with upper bowel contents, all contribute. Quite apart from these, it may be caused by uraemia and retro-peritoneal haemorrhage. In this early stage, resting the bowel by re-establishment of gastric suction and parenteral fluids is often successful in allowing the return of tone. In fully established ileus, i.e. paralysis resulting in physiological obstruction, there is an out-pouring of fluid into the gut, often amounting to 4–5 l. in 24 hours, and this is accompanied by a loss of a variable amount of anions and cations. In a typical case the loss may amount to Na 200–300 mequiv., Cl 150–250 mequiv. and K 20–30 mequiv. in 24 hours.

Surgery offers little in the presence of a paralysed gut and the exhibition of drugs such as prostigmine, pantothenic acid or pituitrin is like whipping a tired horse. However, the distended loops may become acutely kinked one on another, and then mechanical obstruction is superimposed on the physiological one already present and this will lead to localized distension of gut which may be visible through the abdominal wall.

On two occasions I have been successful in the use of operative decompression of grossly distended gut due to this cause. Exploration, under local anaesthesia if necessary, will allow suction decompression to relieve the mechanical element of the obstruction, prevent vascular embarrassment, avoid possible gangrene and encourage the restoration of muscular tone. However, the main essentials of management are the restoration and maintenance of fluid and electrolyte balance. This involves the measurement and analysis of all urine, vomit, aspirates and stools, followed by the accurate replacement of these losses by the intravenous route.

It is in cases with unknown losses into the lumen of the bowel—as well, perhaps, as into the peritoneal cavity—that potassium loss may not be suspected, since depletion of cellular potassium may be present even though serum and urine levels are normal. Cellular potassium may be measured by muscle biopsy, red-cell analysis or by radio-isotopes, but these methods are too intricate for emergency purposes. Potassium depletion will aggravate ileus and lead to general atonia affecting smooth and skeletal musculature as well as of the myocardium. Repeated vomiting alone will also cause hypokalaemia, since loss of gastric HCl results in a rise in plasma bicarbonate with consequent rise in pH. This leads to hypoventilation which tends to restore pH to normal. Throughout, there is an inevitable loss of potassium via the kidneys in an attempt to conserve H^+ ions. After repletion of water, Na and Cl, the raised plasma bicarbonate may persist with further potassium depletion.

Entero-colitis

By this expression one refers to the condition in a patient who, about 4–5 days after operation, suddenly develops an almost cholera-like diarrhoea, so that within a few hours he becomes distressed, severely dehydrated and collapsed. This condition has been variously called acute entero-colitis, pseudo-membranous enteritis or entero-colitis, necrotizing enteritis or antibiotic entero-colitis. A fairly common feature is the passing of sheets or complete casts of the mucous membrane of the gut, and autopsy in fatal cases reveals full thickness necrosis of wide areas of the mucous membrane. These particular pathological features may be associated with several non-surgical diseases such as bacillary dysentery, paratyphoid fever or uraemia; it may also follow operations other than those for peptic ulcer. Dawson-Edwards and Morrissey (1955) reviewed 35 cases of diarrhoea following partial gastrectomy in a seven-year series of 1,700 patients at the Queen Elizabeth Hospital. In 22 of these the diarrhoea was mild, in 8 it was severe, and 5 died. One must therefore be constantly alert to the potential seriousness of immediate post-gastrectomy diarrhoea.

In many cases the exact genesis is not clear, but it seems reasonable to suspect infection. However, it is not easy to recognize unusual organisms in stools, and not every hospital is equipped for all agglutination tests. Although staphylococcus was suspected in the cases of Dawson-Edwards and Morrissey, it was proved in only one, and they could trace no relationship to antibiotic therapy at all. Water and food were also investigated as a source of infection, with negative findings. Suppression of certain groups of organisms by antibiotics may allow other hitherto harmless ones to multiply, gain supremacy and cause serious infection. There is also the fact of cross-infection by an antibiotic-resistant staphylococcus, although it has to be admitted that cases of post-operative enteritis occurred long before sulphonamides or antibiotics were discovered. Nevertheless, it is now generally felt that these cases of necrotizing enteritis are nearly always of staphylococcal origin, often associated with the unnecessary and therefore unwise exhibition of penicillin. More recently, the occurrence of infection by moniliasis has also been recognized, again associated with uncalled-for routine antibiotics. Indeed, perhaps 'antibiotic enteritis' is a reasonable term.

Entero-colitis following partial gastrectomy may prove so serious that instructions should be given to all concerned to report immediately any incident of post-operative diarrhoea, and to arrange for intravenous equipment to be ready. A careful watch is kept on blood pressure since early collapse sometimes develops before fluid stools declare the out-pouring of fluid into the bowel that takes place. Once this diarrhoea starts it may attain cholera-like dimensions and, in order to keep pace with fluid loss and consequent hypovolaemia, it is vital to give fluids intravenously and in heroic quantities—up to 4–6 l. in a few hours. Electrolyte changes at this stage may be too rapid for laboratory investigations to be of use. Plasma helps blood pressure as well as protein loss—the latter, as the result of destruction of cells, is considerable—and solutions of sodium and potassium replenish electrolytes. There is great potassium loss into the bowel which is not reflected in early blood and urine estimations, and this may be replaced by giving 15 mequiv. K/h (up to 6 h) during this emergency period. This fluid replacement is the most important single treatment at this stage, and certainly saved the lives of three patients of the eight reported by Dawson-Edwards and Morrissey. Bruce (1953) wrote well on this subject. Antibiotics, erythromycin being perhaps the best at the moment, should be exhibited, and steroids will help, since supra-renal exhaustion may contribute to the state of collapse. As an example the following case may be recorded.

F. H., aged 52, was admitted to the medical wards of the Queen Elizabeth Hospital in January 1956 complaining of dyspepsia of 11 years duration due to gastric ulcer. In 1946 he had had a haematemesis and over succeeding years the dyspepsia worsened and he lost more and more time from work. A second barium meal in 1951 confirmed the presence of a gastric ulcer. At operation in January 1956 a small gastric ulcer was found on the lesser curve adherent to the pancreas. A Billroth I three-eighths partial gastrectomy and vagotomy were performed. He developed respiratory infection with bilateral basal collapse, and pneumococci and *E. Coli* were found in the sputum. He was therefore put on penicillin and the chest condition improved. Six days after operation he had an attack of diarrhoea. The abdomen was soft and there was no blood in the stools. The diarrhoea was repeated next day but there was neither distension nor vomiting. This continued throughout the next day, the stools being loose and brown but containing no blood. Dehydration was not evident and penicillin was discontinued. By 5 p.m. that day, however, the stools had become watery, with some precipitancy. He was nauseated and actually vomited twice, and there was some distension. He looked pale and drawn, and showed early dehydration. Bowel sounds were exaggerated. Pulse was 96, temperature 100·2°F, blood pressure 120/80. Intravenous fluid was given, and the condition was assumed to be entero-colitis due to penicillin-resistant staphylococcus. Erythromycin 0·25 g, six-hourly was started, and the intravenous fluids were increased to 500 ml/h for the next 4 hours; KCl was added and by 10 p.m. there was some improvement. Total measurable loss by bowel was well over 1 l. Improvement continued the following day when the haemoglobin was 82 per cent; white blood count 13,600; Na = 130 mequiv./l.; K = 4·0 mequiv./l.; Cl 102 mequiv./l.; and serum urea 46 mg/100. Microscopy of the stools failed to show any polymorphs or red blood cells, but there was an excess of fatty acid crystals. There were no recognizable pathogens, and on culture bacterial flora were much modified. He recovered completely, and at follow-up in January 1957 he was very well, all dyspeptic symptoms having cleared up. In February 1962 he was again found to be in excellent health.

Damage to Middle Colic Artery

Under ordinary circumstances, and in primary operations, this should never occur, but in cases where severe inflammatory reaction is present, causing thickening of the meso-colon as, for instance, with a gastric ulcer penetrating in a forward direction, or in the presence of a stomal ulcer or, even more, a gastro-colic fistula, especially following a retro-colic gastrectomy, the process of separating vascular adhesions and identifying various structures may lead to unrecognized damage to the artery. The same applies to second and third operations for other post-gastrectomy problems where adhesions may be dense. Under such circumstances one must remember the risk and watch carefully for any change in colour of the transverse colon. A cyanotic tinge is suspicious, and if there is any doubt the affected part should be excised, reconstructing it by end-to-end anastomosis. I have done this once with complete success. If, for any reason, the patient is not fit for this, it is best to carry out a proximal colostomy.

Jaundice—Injury to Common Bile Duct: Ulcer at the Ampulla

Fortunately, this complication is rare, since most surgeons are fully aware of the risk of injuring the common duct during operation, particularly where the free edge of the lesser omentum is affected by inflammatory reaction, secondary to ulceration of the upper and posterior parts of the duodenum. Maingot (1959) and Bentley (1952) have written well on this subject, and most surgeons make a point of identifying the common duct when dealing with this type of case. Maingot states that 3 per cent of strictures of the common bile duct result from operations for duodenal ulcer.

I know of two cases where the surgeons recognized the severed duct at the time. In one case he proceeded to re-suture it forthwith, and in the second a duodeno-choledochostomy was performed, employing the stump of the duodenum. Both cases recovered completely. The real fear is, of course, damage to the duct by placing a stitch around it without recognizing the fact. When the development of jaundice within a few days of operation makes it obvious that the duct has been damaged, further intervention is called for in order to repair the duct or to carry out choledocho-duodenostomy or choledocho-jejunostomy. A worse mishap is a leak from an unrecognized injury, since bile peritonitis is a dangerous condition, leading as it does to ileus with consequent rapid dehydration and electrolyte imbalance, as already described. Differential diagnosis between this catastrophe and a leaking duodenal stump or pancreatitis is difficult but, in all three, further operation is called for, as soon as the patient has been rendered sufficiently fit, by the same methods as already described.

Occasionally, jaundice, with or without signs of cholangitis, comes on much later; Addison and Fletcher (1962) record such a case in which a bile duct stricture developed two years after partial gastrectomy. These late cases bring up the same questions regarding causation as does delayed stricture following operations on the gall bladder. Possible aetiological factors include stenosing cholangitis and interference with the blood supply to the duct during dissection of a posterior or superior duodenal ulcer. Henley (1952) dissected and injected the blood supply to the common duct in a number of post-mortem specimens, as also did Tudor (1958), both pointing out that although the duct normally has for its blood supply a rich network of vessels, fed mainly by the posterior duodenal artery of Wilkie, this latter vessel is sometimes solitary and an end artery, under which circumstances the blood supply to the duct is more vulnerable; the natural sequel is fibrosis and narrowing. The treatment of late stenosing lesions of the bile ducts is always difficult since reaction in the tissues may make end-to-end reconstruction of the duct impossible, under which circumstances choledocho-jejunostomy, using a de-functioned loop is, in my opinion, the best solution.

Another very difficult situation concerning the common bile duct is the fortunately rare incident of a chronic ulcer affecting the second part of the duodenum adjacent to the ampulla itself.

This I have encountered once only, in a man in his middle fifties who had a ten-year history of dyspepsia of duodenal pattern, and who then perforated. On exposure, the ulcer was found to involve the second part of the duodenum, having perforated to the lateral side. Examination showed that the ulcer bed was in the region of the ampulla. While exploring the duodenum, the wall separated further from the bed on its lateral side, and the opening of the common bile duct could be seen in the base of the ulcer with bile trickling from it. The situation was a difficult one, especially since the patient was obese. Fortunately, a Ryle's tube had been passed into the stomach prior to operation, so this was steered along the duodenum well beyond the ulcer, and the detached rim of the ulcer was stitched back to the reactionary fibrous tissue on the posterior abdominal wall in front of the vena cava. A drainage tube to below the liver was used. The patient was kept strictly on suction and intravenous fluids for five days and, fortunately, recovered. One realizes how fortunate it was that this was not followed by a bile fistula; a safer method would have been to drain the more proximal common bile duct with a T-tube.

Retro-anastomotic and Other 'Loop-the-loop' Herniations

My first interest in this complication arose in 1948, when a patient of mine, recovering satisfactorily from a three-quarters ante-colic Billroth II partial gastrectomy for duodenal ulcer, was about to go home on the twelfth post-operative day. He suddenly felt faint, looked pale and a little cyanosed, and complained of a sensation of constriction of the chest. The lungs were clear, there was no evidence of coronary thrombosis, and no obvious source for a pulmonary embolism, but there was some guarding in the upper left abdomen. By evening he looked and felt better, but next morning he was somewhat distended. He then developed colicky pain in the left lower abdomen and began to vomit, and it was therefore decided to re-open the abdomen. This was done through the original left paramedian incision. The transverse colon was very distended, and the presenting small intestine was collapsed and plum-coloured. On exploring further, it was found that this was jejunum, and that almost all of it had herniated from right to left through the gap between the gastro-jejunostomy in front and the transverse colon behind (*Figure 8*). By gentle traction the herniated coils were easily reduced, and the colour rapidly returned to normal. The gap was closed by approximating appendices epiploicae to the efferent loop with a few catgut sutures. Next day he was completely satisfactory and from then on his progress continued.

A few months later a similar case was admitted to the Queen Elizabeth Hospital under my colleague, B. N. Brooke. This patient had had an ante-colic partial gastrectomy for duodenal ulcer five months previously, and because he had developed upper abdominal pain and vomiting his general practitioner had diagnosed high intestinal obstruction. On admission, there was mild distension. He was observed while fluid and electrolyte balance was restored, but as intermittent pain continued, operation was decided upon. It was found that part of the greater omentum had passed from right to left through the gap between the anastomosis in front and the transverse colon behind, and had then curled forward round the left side of the anastomosis to become adherent to its anterior surface, thus producing mechanical embarrassment by approximating afferent and efferent loops, though not complete obstruction. Reduction was easy; and the patient made a complete recovery (*Figure 9*).

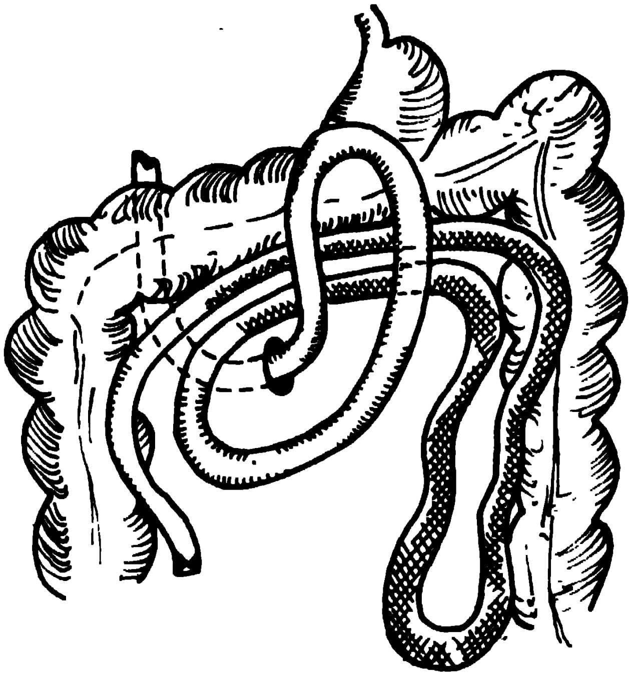

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Figure 8. Efferent loop passing from right to left through the gap and back into the greater sac again

While giving a lecture at the Royal College of Surgeons of England on intestinal obstruction, I mentioned these two cases as rare forms of post-operative obstruction and, after the lecture, a member of the audience produced a sketch which he had made of a somewhat similar experience. Some few weeks previously his chief had performed an ante-colic partial gastrectomy for duodenal ulcer (afferent loop to greater curve) and progress was satisfactory until the seventh day when the patient rather suddenly developed severe abdominal pain and vomiting, and rapidly became collapsed. By this time the surgeon was on holiday, so the registrar decided that a second operation was necessary. He found a puzzling state of affairs, which are best appreciated by studying his excellent sketch made at the time (*Figure 10*). The ileum had herniated from left to right through the same gap as already described, dragging the distal

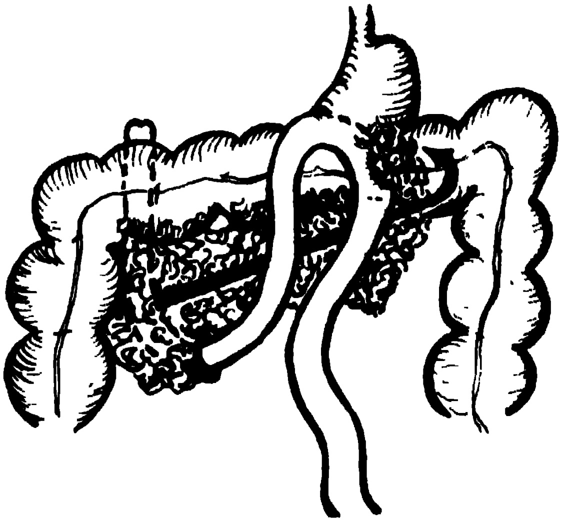

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Figure 9. Diagram showing the omentum having passed from right to left behind the anastomosis and becoming adherent to the front of the stomach and efferent loop

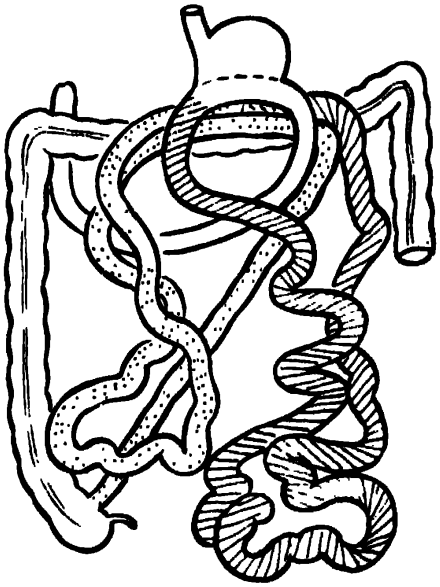

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Figure 10. Lower ileum herniated from left to right through retro-anastomotic gap

60 cm of ileum tightly stretched against the posterior abdominal wall. There was marked congestion of the ileum and, in view of this and because at that time this type of post-gastrectomy internal herniation was a little-known complication, it was thought necessary to take down the anastomosis in order to effect a reduction of what was regarded as some complicated form of volvulus.

Following publication of my lecture (Stammers, 1951), the late Mr W. M. Doolin of Dublin very kindly sent me the notes of yet another example of herniation of small intestine through this man-made hiatus associated with ante-colic gastro-jejunostomy. This was an example of efferent loop passing from right to left through the gap.

Up to this time I had encountered only two patterns of this post-gastrectomy herniation, namely, two cases of efferent loop passing from right to left, and one of omentum from right to left, all following ante-colic reconstruction, and these were reported in 1952; Oldham published another case in 1953. Subsequently, surgeons from all over the world, as well as from this country, very kindly sent me details of similar cases, although they included some different patterns. For instance, there was one case following a retro-colic partial gastrectomy. The patient had progressed satisfactorily for nine days, and then developed sudden epigastric pain and bilious vomiting. Gastric suction was re-instituted with a copious result and relief of the pain. Two days later a small barium meal was x-rayed and, since it showed a 'blocked exit loop', it was decided to re-operate. The anastomosis appeared satisfactory, but a piece of efferent loop some 15 cm from the anastomosis had passed from left to right through the gap bounded by the anastomosis in front, the meso-colon above, the uppermost part of the mesentery below and the posterior parietal peritoneum behind. The herniated loop was withdrawn without difficulty and the gap obliterated by a few stitches; the patient made a satisfactory recovery. At that time, this retro-colic herniation appeared to be quite the rarest kind (*Figure 11*). Since then, however, Peterson's paper (1900) has been brought to light and quoted several times. He described this herniation associated with retro-colic anastomosis, and further reports show that herniation following retro-colic anastomosis is at least as common as after ante-colic operations. As described, the signs and symptoms in retro-colic herniation seem to be similar, though more sudden and severe in onset.

A further series of patterns associated with ante-colic operations was then presented, two from the notes I had collected, and three from West's paper (1953), namely, a long afferent loop, up to 30–

45 cm, herniating from right to left through the retro-anastomotic gap. This is much the most dangerous type, since the blood supply is soon embarrassed as a result of pressure and torsion (*Figure 12*) and, of the five cases from different parts of the world referred to in my paper of 1954, gangrene and perforation had taken place in three, two of which died.

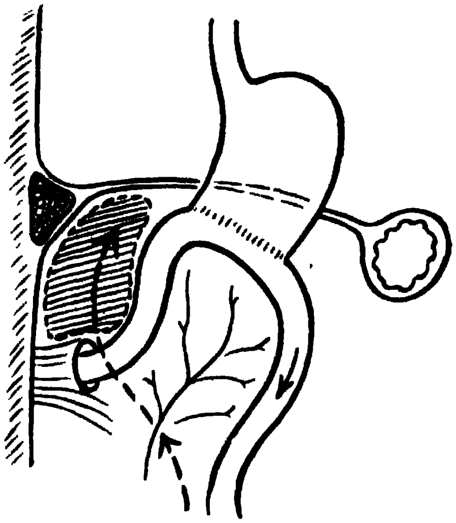

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Figure 11. Herniation in association with a recto-colic gastro-jejunostomy

Since these papers of the early fifties, many more cases have been reported, usually as single ones; during visits to other centres I have heard of a number of others in casual conversation. In major centres performing large numbers of partial gastrectomies, it is very likely that one or other form of this complication will be encountered from time to time. It is impossible to give accurate figures of true incidence, but I should have thought that it was considerably less

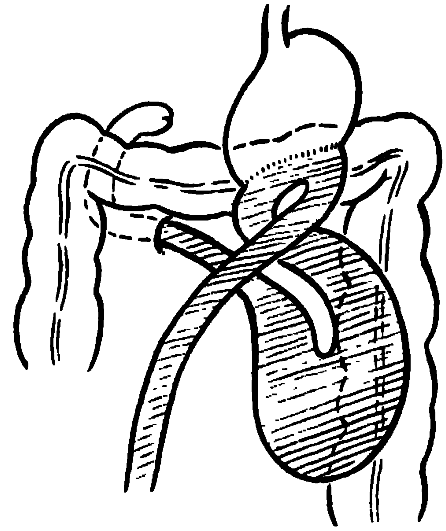

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Figure 12. Herniation of a long afferent loop from right to left through the retro-anastomotic gap

than the 1 per cent suggested by Bastable and Huddy (1960). Yet even if it were only one-quarter of this estimate, this would mean 50 or more herniation obstructions per annum in view of the fact that over 20,000 gastrectomies are performed in this country each year.

In 1954 I suggested that there were six different patterns of these herniations associated with the various forms of ante-colic gastro-jejunostomy, and one with the retro-colic operation, but since then Bastable and Huddy (1960) have collected from world literature (adding 8 of their own) 114 cases of which 46 were retro-colic, 56 ante-colic, and in 10 the type of anastomosis was unstated; the 2 remaining cases involved only the omentum. Although the first case ever to be published was by Buddee in 1897, it was Petersen (1900) who gave the first full account of two cases, one ante-colic and one retro-colic. Bastable and Huddy quote several further patterns to the six I described in 1954, the total list now being:

A. *Ante-colic anastomosis*

(1) Efferent loop from right to left and down into general peritoneal cavity.
(2) Efferent loop from right to left but upwards into lesser sac.
(3) Efferent loop from left to right.
(4) Ileum from left to right.
(5) Most of the small intestine from left to right which, in two cases, included the caecum.
(6) Long afferent loop from right to left.
(7) Efferent loop from left to right, together with afferent loop from right to left.
(8) Omentum from right to left.

B. *Retro-colic anastomosis*

(1) Long afferent loop from right to left.
(2) Efferent loop and most of intestine from right to left.

All the above have been recorded, and one can visualize one or two more. For instance, it seems quite possible for the omentum to pass from left to right in an ante-colic operation, and less so for a long afferent loop to pass from left to right.

Mention of all these patterns is more than of academic interest since, when first encountered, the findings at the second operation can be most puzzling, a number of those mentioned being at first interpreted as instances of volvulus; two of them were not diagnosed accurately until after death. Hoyte, Jayne and Pallister (1957) reported a case of ante-colic anastomosis in which herniation of the afferent loop from right to left was associated with volvulus of the stomach, and in which the grossly distended loop had perforated. Unlike the other reported cases of afferent loop herniation, this loop was a short one, and was the first of this pattern to be recorded. A second operation was performed, the perforation being sutured, the stomach untwisted and the efferent and afferent loops sutured to the posterior peritoneum in such a way as to prevent recurrence; the patient progressed satisfactorily.

Simon (1956) published a case closely akin to, but not identical with, these herniations through the retro-anastomotic gap. In this case symptoms similar to the kind we have been considering developed on the ninth day following a 60 per cent ante-colic partial gastrectomy, and at second operation the afferent loop was found to have herniated into one of paraduodenal fossae.

Considering all these cases, there seems no doubt that it is essential to close these man-made hiatuses whether the anastomosis is in front of or behind the colon, just as one closes any other intraperitoneal gap through which herniation could occur. A second point is that, since the afferent loop herniations are the most dangerous, this is one of the several reasons for avoiding the use of a long afferent loop.

As with other forms of internal hernia, there is always the possibility of some of these being self-reducing and recurrent. From time to time one meets with a patient who states that he has been very well since his partial gastrectomy operation, but that once or twice a year he suffers an attack of severe abdominal pain which tends to increase for several hours, accompanied by vomiting, and then quite suddenly ceases, the patient then returning to normal. The whole incident lasts for 12–24 hours, and never reaches full obstruction. Such attacks could result from a temporary obstruction due to such a herniation and is a possibility which should be kept in mind.

Adhesions Causing High Intestinal Obstruction (an Oddity)

As a diagnosis 'adhesions' seems vague and unsatisfactory yet, from time to time, certain features of a case localize the responsible adhesion fairly accurately. For instance, ten days following a Billroth I operation a patient found that the taking of even small quantities of food produced a feeling of fullness and he started to vomit. There was no distension and bowel sounds were present but the discomfort and vomiting continued, which strongly suggested partial obstruction at the stoma. Since gastric suction failed to improve the situation, operation was decided upon. During the initial operation the falciform ligament and ligamentum teres had been cut and ligated, and at the second intervention it was found that the upper stump of the latter had become adherent to the upper part of the anastomotic line and had drawn it up towards the liver, thus kinking it. This stump was about 4 cm long; since this experience I have made a point, when wishing to cut and ligate this ligament, of doing so flush with the liver.

Oesophageal Stenosis

McKeown (1958), in reporting two cases of oesophageal stenosis following partial gastrectomy, reviewed the literature and commented that there was no mention of this complication in standard textbooks despite the fact that a number of cases have been recorded. He points out that almost all the cases developing oesophageal stenosis after partial gastrectomy have had post-operative complications, including regurgitation, or the incident of some form of obstruction. Like Bartels (1935) he does not think that an indwelling naso- or oro-gastric tube is in any way responsible. This opinion is based on the fact that, although he uses these tubes in the majority of cases, oesophageal stenosis has developed in only two instances out of 1,000 partial gastrectomies carried out by himself (0·2 per cent). Olsen (1948) and Mason and Ausband (1952), on the other hand, think that the use of naso-gastric tubes is significant in the subsequent development of stenosis. In both of McKeown's patients the original operation was of the Billroth II type, and the tube was left *in situ* for 72 hours. On the 20th post-operative day the first case developed burning pain behind the sternum associated with hiccup. Swallowing food caused pain and she experienced a feeling of obstruction at the level of the lower end of the sternum. Barium swallow studies revealed a smooth narrowing at the lower end of the oesophagus and oesophagoscopy showed inflammatory changes. Dilatation of the oesophagus was carried out with only temporary relief, so she was re-admitted and the former Billroth II gastrectomy was converted to a Billroth I, and the opportunity was taken to dilate the oesophagus from below. A naso-gastric tube was kept in for the next five days. The patient made an uneventful recovery, and has remained well ever since, with no dysphagia.

In the second case, also a Billroth II three-quarter gastrectomy, a naso-gastric tube was again used. Convalescence was initially satisfactory, but three weeks later he experienced difficulty in swallowing and a sensation of obstruction at the level of the lower end of the sternum. Occasional regurgitation occurred. This continued for five months, during which time he lost over 20 kg in weight, but did not report to his doctor or to the hospital. He was re-admitted nine months after the first operation in a poor condition, and with serious dysphagia. Barium swallow showed a stricture, and oesophagoscopy revealed an inflammatory narrowing. Since dilatation was ineffective, conversion to a Billroth I reconstruction was carried out. A naso-gastric tube was employed for five days, and then a further dilatation was performed. From then onwards, progress was entirely satisfactory and the patient has remained well.

Some authors have suggested a vascular cause for such stenosis (Straus, 1950), while those blaming the tube think that it encourages regurgitation and that it is the acid and pepsin that are responsible. However, McKeown noted in both his cases that there was complete absence of free HCl and that at pH 6·5-7 the probable cause of oesophagitis and consequent stenosis was tryptic activity. He also pointed out marked similarities between his two patients, namely, that both were over 64 years of age; both were debilitated prior to operation as the result of vomiting and loss of weight; and both had pyloric stenosis.

SUMMARY

No matter which particular operation is chosen, the technique must be gentle, precise and accurate. In gastric surgery, perhaps more than in any other, experiences such as those described must be pondered over and memorized, and where points of technique suggest a cause, that technique should be modified accordingly. With the Billroth II type of operation, the following points are of vital importance: the meticulous closure of the duodenal stump; respect for the peritoneal arrangements at the D.J. junction and the lie of the first few centimetres of the jejunum; avoidance of too long an afferent loop (10 cm in the ante-colic operation, and none at all in the retro-colic); attention to haemostasis; and the closure of any man-made gap through which intestine may herniate.

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4

POST-GASTRECTOMY PROBLEMS—EARLY AND DELAYED

F. A. R. Stammers

All forms of partial gastrectomy produce fundamental alterations in the anatomy and physiology of the upper intestinal tract. Following the gastro-jejunal type of reconstruction (Billroth II)—either ante- or retro-colic—food passes directly from a greatly reduced stomach reservoir into the upper jejunum in an almost totally undigested state, without any such mechanism as the pylorus to control the rate. With gastro-duodenostomy (Billroth I) the stomach reservoir is usually bigger than in the Billroth II operation, and food passes by its natural route via the duodenum and is therefore mixed with bile and pancreatic enzymes. However, as in the Billroth II operation, there is no pyloric mechanism, and so food again reaches the jejunum in a less well prepared state than normal. In Chapter 5 the present-day understanding of the physiology of digestion in man is described and the ways in which the different forms of surgical treatment interfere with the physiology of the upper intestinal tract, are discussed.

When discomforts do recur, or develop afresh, after partial gastrectomy they vary greatly in pattern. Some patterns are so precise and constant that they are referred to as post-gastrectomy syndromes and can be related to definite mechanical features, such as a small reservoir, a faulty afferent loop or a partly obstructed efferent loop. Other patterns are mixed and varying, at first seeming to be confused and exaggerated; in fact, they may be genuine, resulting from more than one of these mechanical factors being operative at the same time. With increasing experience these symptom complexes can often be analysed with considerable precision. Obviously, when dealing with such cases it is of vital importance to assess the psychological stability of the patient, and to enquire into home circumstances and working conditions.

Another group of post-gastrectomy patients are reported with features of metabolic disturbance, such as malnutrition, anaemia or, very occasionally, of gross steatorrhoea, and there may be little in the way of upper gastro-intestinal symptoms. These metabolic disturbances result from altered physiology; indeed, they can be reproduced in experimental animals by similar operations.

A further possible factor is that the patient may already have some metabolic variation from normal, such as latent sprue or coeliac disease, which is revealed in the form of post-operative diarrhoea by the changed anatomy following the partial gastrectomy necessitated by his co-incidental peptic ulcer. As an example of variations from normal, Cox (1952) has shown that the oxyntic carpet in the proximal part of the stomach varies in area and richness from one patient to another, and that victims of duodenal ulcer tend to have a richer carpet and larger stomach than average. It is now being realized that the gastrin producing area varies similarly. The recognition by Zollinger and Ellison (1955) of the relationship between a non-beta cell tumour of the pancreas and the excessive secretion of highly acid gastric juice suggests a possible clue to the development of repeated stomal ulcers which sometimes bedevils patient and surgeon alike. In a recent case of Ellison-Zollinger tumour, on whom I operated (Rawson and colleagues, 1960), the nocturnal gastric secretion amounted to 2 l. with pH 1·7. The patient, incidentally, is still in normal health 3½ years after operation, although no more than removal of the tumour was done. Summerskill (1959) showed that general hyperplasia of these cells throughout the pancreas also caused excessive production of acid, with similar results. Tumours of the supra-renal, pituitary and parathyroid glands may also rarely be associated with gastric hyperacidity and intractable ulceration (Cooke and colleagues, 1960).

As the result of a careful study up to 1960 of 61 patients with various post-gastrectomy problems developing subsequent to the immediate post-operative period, will present examples of all the phenomena referred to above. They can be classified, first, into those that develop soon after the patient returns to active life and, secondly, into those that come on after the patient has had several years of good health. Before discussing these two groups, however, a few points will be stressed concerning the first few weeks after operation.

FIRST FEW WEEKS

It is important after any operation to talk to the patient about his first few weeks after leaving hospital, and this is particularly so after partial gastrectomy. He should be warned that he will probably experience a few minor discomforts during the first few weeks, but he should be reassured that they will clear up quite soon. It is wise to discuss convalescence in relationship to home circumstances, making sure that they are suitable regarding rest, relaxation and nicely prepared food. The patient should be told when he can return to work which depends, of course, on the nature of his occupation. Work involving irregular hours or a rotating shift system should be changed, if possible, since regularity of meals is important. The business executive will probably become restive unless allowed to return to his office quite soon; for him, as also for the patient with sedentary work, a month's convalescence is about right. The factory worker requires about 6–8 weeks, but the miner working at the coal face needs up to about three months. Enforced inactivity for longer than these approximate times keeps up an atmosphere of invalidism and, therefore, lack of confidence.

It is essential to communicate with the patient's doctor and to ask him to contact his recently returned patient. He should be given details of operative findings, operation performed, and advice regarding diet, convalescence and return to work. Such details are necessary and usually appreciated, since there are few general practitioners who have more than about a dozen partial gastrectomy cases on their books.

Even though the ulcer pain has been cured, it would be surprising if, in view of the changed anatomy and physiology already mentioned, patients did not at first sense that things were different inside. They find that they cannot eat as much as before, or that they experience slight nausea or regurgitation, and naturally feel somewhat apprehensive. These sensations are more likely after major resections. One of the most common complaints is the feeling of fullness during meals and the fact that they cannot eat as much as other members of the family. This tends to improve quickly, but advice to have small meals, and to take drinks between meals rather than with them, combined with general reassurance, will usually help them to regain self-confidence. After the first few weeks they can usually eat the same food as the rest of the family, but if a patient still tends to feel full rather easily, the régime of small frequent meals should be pressed.

Another thing that tends to upset some patients is the realization that their bowel habits have changed, the tendency being towards more frequent actions or looser stools. Reassurance is again usually all that is necessary; many patients welcome the change.

In the early weeks some patients complain of attacks of a feeling of weakness, faintness, dizziness and sweating after taking food, sometimes even necessitating lying down. These phenomena amount to the 'dumping syndrome', and are particularly liable to be these attacks varies greatly but the majority clear up completely within a few weeks, only a minority progressing to the truly incapacitating form which is discussed on p. 68. The Birmingham series, reviewed by Brookes, Waterhouse and Thorn (1960), contained very few of the fully developed 'dumping syndrome', even though milder examples were often encountered during the first few weeks. Reports vary greatly on this point; for instance, Muir (1949) stated that 75 per cent of 124 cases had suffered at some time from dumping, 15 of which were unable to start work for five months. Gilbert and Dunlop (1947) reported 17 instances out of 45 gastrectomies (38 per cent), whereas Lake (1948) had only 20 out of 615 personal cases (3·3 per cent). During early weeks these discomforts can be helped by reducing the intake of carbohydrates, especially sugary ingredients; and since distension of the efferent loop is a major factor, anything reducing bulk, yet at the same time maintaining caloric sufficiency, will be helpful.

Yet another symptom occasionally complained of during the early weeks is early morning nausea and, sometimes, the vomiting of bile. Lake (1948) found that this early morning nausea was more common in patients who slept on their left side and suggested that it resulted from irritation of stomach mucosa by bile which, in the absence of a pyloric sphincter and encouraged by lying down, entered the stomach reservoir from the afferent loop. These symptoms usually disappear on assuming the upright position or after the first few mouthfuls of food. Incidentally, it is not uncommon to meet post-gastrectomy patients who, though otherwise well, declare that they do not want breakfast. The inflow of bile into the stomach may be related to the observations of Cox, Doherty and Kerr (1958) on the size of the gall-bladder after gastrectomy.

They showed that in 14 out of 15 patients the gall-bladder had become considerably dilated within two weeks of operation, and that the cholecystogram six months later showed that this was progressive; the size of the gall-bladder after vagotomy is mentioned in Chapter 11. They also demonstrated that in most post-gastrectomy patients the gall-bladder empties more rapidly after fatty meals than prior to operation; they relate this to the rapid emptying of the small stomach which is associated with gastro-jejunostomy. Scott and Whiteside (1956), using intravenous biligraphin, also demonstrated enlargement of the gall-bladder after partial gastrectomy and, in addition, showed apparent spasm of the sphincter of Oddi which prevents the normal state of affairs, namely a virtually continuous slow trickle of bile until a meal is taken, and then a rather sudden emptying into the afferent loop. Both dilatation of the gall-bladder and altered rhythm of emptying probably result from interference with branches of the vagus nerve caused by operation, the more radical the gastrectomy the more likely is damage to the hepatic branch of the nerve. All these features are of special significance when the afferent loop is longer than the average (10–15 cm). As with other post-cibal discomforts of the first few weeks this bilious vomiting tends to settle down, but if it continues these need to be differentiated from those resulting from mechanical embarrassment of the afferent loop, which is discussed on p. 79.

Since many of the initial post-operative discomforts may take several months to disappear, it is wise not to include first year cases when assessing results; a good deal of adjustment has to take place. However, the patient of ordinary fortitude soon regains his confidence and loses his discomforts. It is during these early weeks, also, that patients having psychological instability and who are, therefore, really unsuited to surgical treatment, reveal themselves. When reviewing failures, one realizes that some should never have been subjected to operation, and one grows wiser in one's selection. Patients describing their symptoms in exaggerated and fanciful terms and at great length do not react well to discomfort of any sort. This also applies to the man of intemperate habits, admitting that he smokes up to 60 cigarettes a day, and drinks as much as he can get; he will very probably continue to do so after his operation.

The more one sees of peptic ulcer patients, the more one is able to sense this lack of stability or fortitude when it exists. At the same time, the importance of environment in the form of a happy home and contentment at work, should be remembered. When faced with a persistent post-gastrectomy problem in a patient who seems to react in an exaggerated way, I ask the opinion of one of my psychiatrist colleagues. Sometimes he says 'if there is a correctible mechanical factor present, this man will respond favourably', but on other occasions he will say 'don't operate on this patient; he will complain of the scar'.

I also believe that before operation is suggested patients should have suffered their ulcer pain sufficiently long to realize its severity and the degree of distraction it may cause. Otherwise they will forget their short-lived ulcer pain and attribute any residual discomfort to the operation. I stress this because a few years ago general practitioners were getting so confident in surgical treatment that they were referring cases to surgeons within about six months of onset. My own experience makes me believe that, except for perforation or bleeding, two years is about the optimum time, and that any subsequent minor discomforts will then be accepted as a worthwhile exchange. I believe that the less physiologically disturbing operation of vagotomy and pyloroplasty carries less risk of even these minor discomforts.

EARLY COMPLICATIONS

By 'early' complications I refer to the patient whose sensations and anxieties of the first few weeks following operation have not settled down spontaneously, and who continues to complain of discomforts, in spite of the original ulcer pain having been cured.

Little Stomach Syndrome

A few patients continue to complain of symptoms associated with a small reservoir and conveniently termed the 'little stomach syndrome'. The common complaint is that they continue to be unable to take normal-sized meals, and even when modified by omitting bulky ingredients, avoiding drinking with food or taking more frequent meals, they are unable to take sufficient to maintain weight and energy. Any attempt to take more causes fullness, sometimes amounting to pain, and even dumping and vomiting. The less intelligent ones fail to realize the significance of six comfortably small meals instead of four uncomfortably large ones; it is the small reservoir that is responsible.

The features of dumping often accompany the discomforts of a small reservoir. This is not surprising since a small reservoir leads to a more rapid passage of solid food into the upper jejunum. It is not uncommon at a second operation on a patient having had a partial gastrectomy in the past, to find the first 20 cm or so of the efferent loop hypertrophied and dilated as if acting as an accessory reservoir in continuity with the remains of the stomach. This may be effective so far as increased reservoir is concerned but, as is discussed on p. 68, the presence of hypertonic food in the upper jejunum may lead to the phenomena known as dumping.

Duncan (1955), while working with me, measured the capacity of these reservoirs following the gastro-jejunostomy type of reconstruction. He did this by feeding the patient with a potato-barium mixture until the full feeling was produced, checking by x-rays any outflow through the stoma. He found that about 500 ml was the critical capacity and a smaller reservoir tended to be associated with discomfort. Incidentally, in a recent paper (1961), I quoted this wrongly as 250 ml. He also assessed the capacity by the use of a balloon in the reservoir, confirming 500 ml as the volume below which the 'little stomach syndrome' was likely to develop (*Figure 13*) It is interesting to note that in two patients he actually reproduced

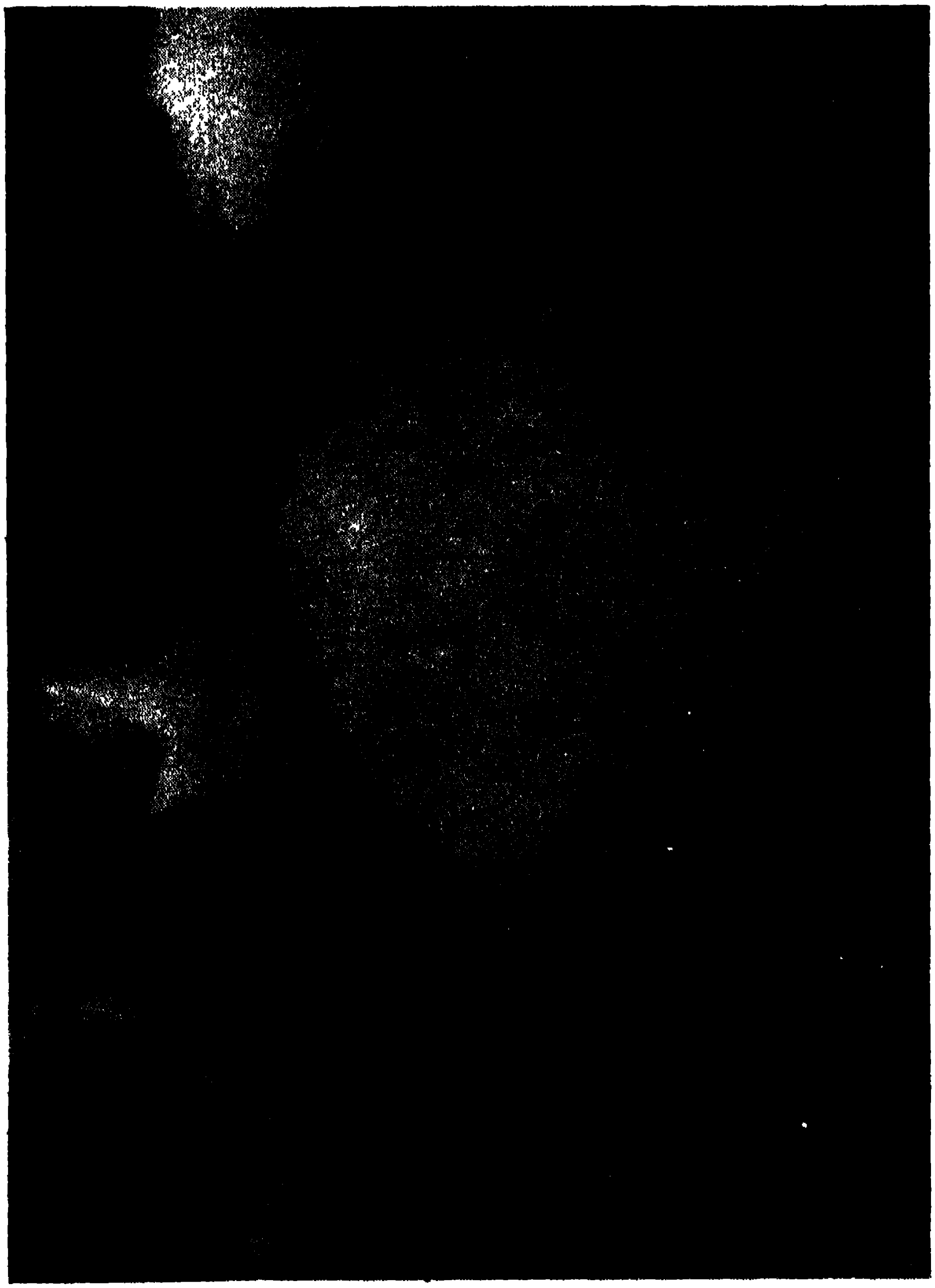

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Figure 13. Balloon measurement of little stomach

the symptoms of 'dumping' by inflating the balloon as it lay in the small stomach stump. This may, of course, have resulted from transmitted distension of the efferent loop. Most patients, as already stated, will learn to live with their diminished capacity by acceptin that they must take frequent small meals, but if they continue t lose weight and energy, the situation can be much improved b

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Figure 14. Henley loop between small gastric stump and duodenum

converting the gastro-jejunostomy operation into a Billroth I, enlarging the stomach reservoir by the interposition of a 15–20 cm loop of jejunum, iso-peristaltically placed and with vascular pedicle intact, as first described by Henley (1952). Vagotomy should be added in order to eliminate the neurogenic element of gastric secretion, thus minimizing the tendency to develop ulcer in the jejunal loop. The increased reservoir capacity probably does not amount to more than 200–300 ml and part of the success of the operation is because it allows gastro-duodenostomy without tension on the suture line. The chief advantage is that it is a more physiological arrangement (*Figure 14*). The following is a good example.

In 1952 H. C., aged 49, was treated elsewhere for duodenal ulcer and mild stenosis by a major Billroth II type partial gastrectomy. After the operation, he developed a different and more troublesome set of symptoms consisting of a feeling of post-prandial distension after meals, and dizziness and fatigue. In 1955 he was sent to the Queen Elizabeth Hospital complaining of fullness after meals, loss of 18 lb. in weight, and fatigue. There was little true pain. Haemoglobin was 102 per cent. Faecal fat amounted to 12 g/day. Glucose tolerance test showed a high rise and rapid fall-away. X-ray of barium meal revealed virtually no stomach reservoir; there was no ulcer. A diagnosis of little stomach syndrome was made, with mild afferent loop, and an element of efferent loop, syndromes together with some disturbance of fat metabolism. Operation was decided upon, at which the Billroth II anastomosis was taken down, the jejunum joined end-to-end, and a conversion to a Billroth I anastomosis carried out, the stomach reservoir being enlarged by the interposition of a 15 cm segment of transverse colon isoperistaltically placed. In May 1956 he reported that nausea and regurgitation had ceased, although he still complained of some distension. In February 1962 his doctor reported that he had not complained of his stomach for some time and that he is in reasonably good health.

Dumping Syndrome

The expression 'dumping' refers to a precise group of sensations coming on after food, usually quite soon, but sometimes after an interval of 2–4 hours. Faintness, dizziness, weariness, an urge to lie down, sweating, palpitations, sensation of flushing (although the patient often looks pale) are all included in this syndrome. In their fully developed form such attacks are impressive to see. The patient looks like a diabetic on insulin who has missed a meal, or like someone undergoing the Hollander test for completeness or otherwise of vagal section (Brooke, 1949). For this test the patient receives 10–20 units of insulin intravenously with the object of producing a state of hypoglycaemia. The features of dumping are very similar to the signs and symptoms of hypoglycaemia. However, not every attack of dumping is associated with hypoglycaemia; more often it coincides with a phase of hyperglycaemia.

Several factors have been shown to be associated with 'dumping' and, in some patients, more than one of these can be shown to be operative at one time. The following may contribute to the syndrome, and it will be appreciated that distension of the efferent loop plays a part.

(1) In 1948 Brain, while working with us, showed that if a balloon resting in the upper jejunum was inflated it produced the features of dumping, even to fainting.

(2) Mix (1922) argued that rapid emptying of food into the upper jejunum, the rate being accentuated by a small stomach, caused distension and that this resulted in a state akin to shock, just as pulling on the jejunum during operation under local anaesthesia will cause shock.

(3) Machella (1950) also thought that rapid distension of the jejunum by food was responsible, but considered that it was augmented by the rapid out-pouring of *succus entericus* consequent on the rapid arrival in the jejunum of hypertonic untriturated food.

(4) A different mechanism was suggested by Gilbert and Dunlop (1947) who noticed that carbohydrate, and especially sugary foods, were most likely to produce attacks in a victim of the syndrome. Gilbert and Dunlop suggested that it was the rapid absorption of carbohydrate from the efferent loop which used up circulating insulin, and that this stimulated the secretion of further insulin at a time when carbohydrate had already been metabolized, thus leading to hypoglycaemia, sometimes as low as 40 mg per cent. This theory satisfactorily explains 'dumping' coming on several hours after meals, and hypoglycaemia can often be shown to accompany this delayed form. Much more commonly, however, dumping comes on during or within half-an-hour of a meal, which then coincides with a state of hyperglycaemia.

(5) Capper and Butler (1951), impressed by the fact that the feeling of faintness was promptly relieved by lying down, thought this to be strongly suggestive of a mechanical factor, just as pulling on the jejunum causes faintness. They pointed out that, with major gastrectomies at least, the remnant of stomach was left with very little support, such structures as the left gastric artery and the gastro-hepatic omentum having been detached during operation, so that when the stomach reservoir contained food, it literally hung on the oesophagus and diaphragm; hence the relief brought about by lying down. They suggested various ways by which the stomach and anastomosis could be attached to the

posterior abdominal wall, thus reducing this drag. I do not think that further experience bears out this hypothesis.

(6) Smith (1951) studied serum potassium and found that victims of true 'dumping' had a passing hypokalaemia; he also showed that there were changes in electrocardiograms during attacks which he attributed to low serum potassium. However, it has since been shown that hypokalaemia develops after the symptoms have subsided.

(7) Le Quesne, Hobsley and Hand (1960), like Machella, were impressed by the great out-pouring of *succus entericus* that took place, but thought that its effect might be of a more fundamental nature than distension. By giving 175 ml of 50 per cent glucose by mouth they precipitated attacks in susceptible patients. They found that in such patients there was a fall in plasma volume of up to 20 per cent, with an average of 13·1 per cent. In a second series of experiments they showed that these dumping symptoms could be greatly modified by giving soluble insulin subcutaneously some time before the glucose was taken, and that there was a coincident lessening of reduction in plasma volume. It is questionable, however, whether insulin has a therapeutic place in victims of dumping from this cause.

(8) More recently, Cox and Allan (1961), relating the feeling of faintness to hypotension, gave a different explanation, namely, failure to compensate by peripheral vaso-constriction for the normal diversion of blood to the splanchnic areas taking place during digestion, especially when in the sitting or standing positions. Following a meal they studied blood pressure and blood flow in the feet in both erect and horizontal positions, and found that in some patients the normal peripheral vaso-constriction fails to take place, and that there is a fall in blood pressure when the patient stands or sits, and that this coincides with the attack. The maximum fall recorded was 20 mm Hg, which perhaps seems surprisingly little to account for faintness. In two of my own cases we were unable to demonstrate hypotension during attacks.

(9) Cox and Allan (1961) have also described in two cases the radiological appearances of a barium meal during actual attacks of dumping; there was seemingly complete inertia of the bowel, i.e. a complete cessation of all movement in both stomach and small intestine, and even if due to sympathetic activity, the coincidence is an interesting observation.

These different factors can be placed under the headings distension, hyper- or hypo-glycaemia, hypovolaemia, hypotension, hypokalaemia, mechanical and inertia and, when faced with a case of 'dumping', they at least give a guide to lines of investigation. My own view is that distension and hypovolaemia are the two most important factors. Simple measures may be sufficient, such as avoiding bulky meals and sugars. However, where unrelieved, symptoms associated with persistent 'dumping' are incapacitating, and the patient begins to feel insecure and demands that something more be done. Since mechanical distension, and the various metabolic consequences of early and uncontrolled arrival of undigested food in the upper jejunum, are obviously initiated by gastrojejunostomy and aggravated by a small stomach reservoir, it is reasonable to convert the Billroth II operation to a Billroth I; where the stomach remnant is very small, say one-tenth of the original, it is reasonable to use a Henley loop in order to enlarge it as well as to minimize tension at the new anastomosis. I have done this on four occasions, and there is no doubt that all the unpleasant symptoms are markedly improved. The following is such a case:

R. M. T., a man aged 38, was transferred in September 1959 from the Smethwick Centre for Nervous Diseases, where he had been investigated because he had suffered from attacks of unconsciousness coming on 10 min after meals ever since he had had partial gastrectomy for duodenal ulcer at another hospital in 1953. These were especially likely to occur after taking sweet food and, particularly, sweet fluids. The attacks simulated sleep and lasted up to 30 min. There was no complaint of pain. The central nervous system was normal, including electro-encephalography. During attacks blood sugar was low and at the end of 2½ hours was 50 mg/100 ml; threatened attacks were prevented by giving glucose intravenously. Barium meal showed a Billroth II type gastrectomy with a small reservoir, and emptying of the reservoir was described as being exceptionally rapid, the head of barium reaching the lower ileum in 25 min. A full lunch, followed by a cup of sweet tea and then walking about the ward for 5 min, caused sweating and fatigue and a desire to lie down. Blood pressure during this was 170/110, pulse was 120 and respiration was 24. The giving of 2·5 g glucose by intravenous route restored him to normal, blood pressure becoming 130/90 and pulse 88. It must be admitted that the onset of the 'dumping' within 10 min of a meal, associated with hypoglycaemia and relieved by 2·5 g glucose, is not typical. Nevertheless, it was decided to convert the Billroth II operation to Billroth I. At operation on 19.10.1959 an ante-colic Billroth II partial gastrectomy was revealed, with a small reservoir and long afferent loop. There was no stomal ulcer. Conversion to Billroth I was carried out.

When seen in March 1962 he said that he was 'reasonably well', and was at work. He suffered some retro-sternal discomfort, but had only had two fainting turns in 2½ years.

Despite all that has been said, it is well to realize that patients do not necessarily suffer 'dumping' even though investigations show that one or more of the above factors are present, such as hypovolaemia or hypoglycaemia. It should also be pointed out that fainting attacks in a patient who has had a partial gastrectomy operation may be attributed, mistakenly, to the operation, yet may really be of completely different origin. For instance, a man of 73, having had partial gastrectomy for long-standing duodenal ulcer, developed fainting attacks some six months later. Apart from these, he declared that he was, in every way, fitter than he had been for years and was completely free from ulcer pain. On investigation, the attacks proved to be due to vertebral artery narrowing, the result of athero-sclerosis. I have also seen a patient who had never had any stomach operation at all, describing the symptoms of 'dumping'. He had had left lower lobe lobectomy for carcinoma of the bronchus, and had developed the new symptoms a few months later. Might this be an example of the 'carcinoid syndrome'?

Intestinal Hurry

Though relieved of their ulcer pain and feeling generally better, some patients declare that they continue to have the looser stools and more frequent bowel actions that started soon after the operation. They admit that this causes little inconvenience, although a few point to the lower abdomen and say that they feel as if food has reached that point very soon after taking it. If a barium meal is x-rayed, it is found that in some patients the barium has truly reached the caecum within 30 min (*Figure 15*). It should be mentioned, however, that it is becoming increasingly recognized that barium alone is not treated by the bowel in the same way as food mixed with barium, and studies concerning this are being carried out in our department. This alteration of bowel habit is another consequence of the rapid arrival of lumpy undigested food in the upper jejunum, which causes exaggerated peristalsis and hurry. It may lead to malabsorption, with loss of weight and energy, under which circumstances further investigations and treatment are called for; where nutrition is satisfactory, simple measures such as small frequent meals, and avoiding tough fibrous fruits and vegetables will help. Rarely one may have to resort to drugs, e.g. probanthine or hexamethonium.

Steatorrhoea—Early and Delayed

In some patients the looseness of stools does not settle down but worsens, amounting to frank diarrhoea, causing inconvenience, distress, and associated with flatulent dyspepsia and steadily worsening health. The stools may be bulky, pale, soft and offensive and float on water; these are characteristics of steatorrhoea. On the other hand, steatorrhoea is sometimes associated with constipation; a disturbance of fat metabolism may only be discovered by the incidental discovery of raised faecal fat. There is also the type of steatorrhoea which develops later, after several years of satisfactory health.

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Figure 15. Intestinal hurry

When faced with such cases, full differential diagnosis has to be made between coeliac disease (gluten sensitivity), sprue, the blind loop and other malabsorption syndromes, idiopathic steatorrhoea and pancreatic disease—and milk sensitivity must not be forgotten

During the past 20 years much original and fundamental research on fat metabolism has emerged from this School (Frazer 1952, 1961). We made a study in Birmingham of the results of tota gastrectomy for carcinoma, 14 or 15 years ago. This was at the time when the aftermath of total removal of stomach had not been foreseen; later experience showed that although occasional successes were obtained so far as comfort and nutritional state were concerned, the majority of patients were left in a wretched state. They were unable to take more than very small meals without severe discomfort, they suffered from noisome diarrhoea, lost weight and energy rapidly, and became anaemic; it was hardly an exaggeration to say that they were dyspeptic wrecks. We studied particularly the nutritional disturbances that seemed to affect a high proportion of total gastrectomy cases, and soon came to the conclusion that there was often a serious disturbance of fat metabolism, resulting in steatorrhoea, and that this was largely responsible for the state of malnutrition (Brain and Stammers, 1951). The different causes of steatorrhoea are dealt with in Chapter 10.

Of interest to the surgeon is the fact that these observations suggest that steatorrhoea following partial gastrectomy is related to several factors, all initiated by the changed anatomy. Certainly, the depression of pancratic secretions following the Billroth II gastrectomy, together with partial inactivation of enzymes, play an important part; the difference between long and short afferent loops is also important, and this supports our original suggestion made in 1951 of a holding-up process in the afferent loop preventing the free admixture of pancreatic enzymes and food at the optimum time, i.e. as it passes from the stomach reservoir into efferent loop. Obviously the longer the loop, the more it acts as an interruption or retardation and Brain's expression 'pancreatico-cibal asynchrony' certainly describes its operative background. It is a fact that the very long afferent loops, say 45–50 cm, that are still being made by some surgeons today, are liable to be associated with disturbance in fat metabolism. Kinsella and Hennessy (1960) have suggested that the duodenum and afferent loop together form a blind loop, and that steatorrhoea is an example of the blind loop syndrome with its recognized malabsorption phenomena. In view of the fairly brisk yet intermittent, flow of pancreatic secretion and bile that passes through it, I find it difficult to think of the duodenum and afferent loop as quite the same as a blind loop. Nevertheless, Kinsella has shown that organisms are frequently present, and this may add another factor; we have confirmed this latter observation. With these explanations one would expect these disturbances of fat metabolism to declare themselves soon after operation, and this is true, although it may be symptomless and only revealed by laboratory investigations (this is dealt with in Chapter 10).

Some cases develop clinical steatorrhoea after a lengthy interval, as in the following case.

In 1952, W. G. then aged 58, was treated elsewhere for duodenal ulcer of six years standing by partial gastrectomy of ante-colic type, afferent-loop-to-greater-curve. In due course he returned home, and despite having lost the pain, he said that he felt vaguely uncertain of himself and was generally dissatisfied, even though his appetite was good. He did no regular work for 2½ years, merely performing odd jobs. In 1956 he developed alternating diarrhoea and constipation, and first came under my care at the end of 1960. During the attacks of diarrhoea the stools were pale and frothy. He was thin but otherwise looked fit. Haemoglobin was 88 per cent. Liver function tests were normal. Daily faecal fat content varied between 20 and 40 g on ordinary ward diet. Barium meal showed that the gastric remnant emptied slowly and that there was some retention of barium in the afferent loop. There were frothy faeces in the colon, and the picture was typical of steatorrhoea. A jejunal biopsy was normal.

In view of these periods of constipation he was treated with Dulcolax and this made him feel much better. He was therefore sent home. In April 1961 he was re-admitted, complaining again of alternating constipation and diarrhoea, with distension, vomiting of bile, pain in the left hypochondrium and what he described as a heavy feeling all day. Operation was advised. The very mobile caecum was found to be adherent to the anastomosis and was distended. This was separated, and the Billroth II operation was converted to a Billroth I, and he made good progress. Fat studies after operation showed that on ordinary ward diet faecal fat was now only 2 g in 24 hours. The diarrhoea had completely cleared up. In February 1962 he said, 'I can only tell you how wonderful it is to feel well'.

We have encountered a further three patients in whom severe steatorrhoea developed some time after the original operation. The operations were performed at other hospitals and the patients seemed to be in excellent health for several years, and then over the course of a few months began to have discomfort, distension and diarrhoea, the latter rapidly becoming characteristic of steatorrhoea. In each case the findings were the same, namely that the afferent loop was longer than customary and, over the years, had become dilated until in two cases it held as much as 150 ml of bile and pancreatic secretions; in the third case, it held double this amount In addition to the dilatation there was considerable concertina'ing of the afferent loop resulting from enveloping adhesions, so that eventually, and relatively quickly (within a few months), it began to act as a sump, in effect sequestrating that which had hitherto been mixed adequately with gastric contents as they passed into the efferent loop. X-ray studies may reveal this (*Figure 16*). With

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Figure 16. 'Sumping'

this element of obstruction and stasis in the afferent loop, certain features of the 'afferent loop syndrome' developed, namely, fullness amounting to discomfort, and pain soon after meals, relieved only by the vomiting of pure bile, sometimes amounting to 300 ml or more. Sometimes the vomit consisted of undigested food heavily mixed with bile, this latter feature being almost certainly due to distortion of the stoma by the distended afferent loop impinging on the efferent part of the stoma.

A rather more dramatic onset, and due to a different cause, was seen in a man aged 57, who had enjoyed good health for five years following a retro-colic Billroth II gastrectomy performed abroad for duodenal ulcer. Then, within a few weeks he experienced increasing discomfort towards the end of meals, and vomited occasionally. He developed a change in bowel habit and noticed that his more frequent stools were loose, pale and bulky. The post-cibal discomfort increased and he said that recently he could see a smooth tense swelling in the epigastrium within a few minutes of eating, and with it he suffered definite pain. He was tall and thin, and it was easy to see the mentioned swelling developing quite quickly on taking food. It became tense and tender and never completely disappeared between meals. He was investigated; haemoglobin was 83 per cent; occult blood was present and faecal fat over three days showed an average of 14·3 g in 24 hours. At operation the condition proved to be carcinoma of the stomach stump which almost completely blocked the afferent loop and narrowed the efferent loop orifice (*Figures 17* and *18*). The swelling referred to was retro-peritoneal and consisted of duodenum and afferent loop, and it contained about 150 ml of turbid yellow fluid. Palliative entero-enterostomy was carried out, and for 3-4 weeks he was more comfortable, faecal fat falling to 9·6 g daily. This level was maintained even at the end of three months, although he died five months after the operation from general carcinomatosis.

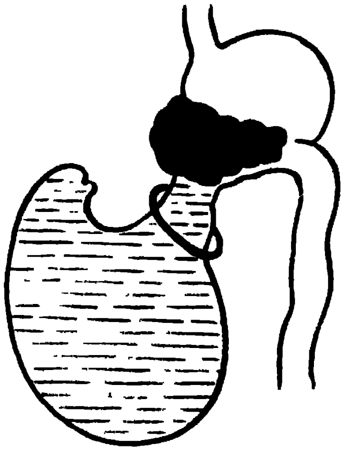

Figure 17. Carcinoma of stomach stump causing obstruction of stoma

These four cases are examples of what I referred to earlier as nature's experiments—in the first three cases the effect of slow obstruction of the afferent loop; in the last the effect of relatively acute obstruction of the afferent loop. Butler's observations (1961) on the differences in fat absorption between long and short afferent loops might also be likened to a planned experiment.

Thinking in terms of the two extremes—on the one hand the patient who suffers nothing although examination of stools reveals that he is losing more fat than normal and, on the other, the victims of delayed steatorrhoea, such as the first three cases mentioned above—it seems reasonable to argue that in between these extremes there may be various degrees of slowly progressive dilatation of the afferent loop, perhaps with additional mild obstruction due to adhesions, which will cause varying degrees of disturbance of fat metabolism.

Figure 18. Carcinoma of stomach stump causing obstruction at stoma affecting particularly the afferent loop side

Osteomalacia—A much rarer complication and often associated with long-standing steatorrhoea of a severe degree, is osteomalacia, sometimes even with spontaneous fractures. This is dealt with in

Chapter 9. I have had two such cases referred to me, both having had nine-tenths Billroth II gastrectomies for duodenal ulcer some years previously. Both developed steatorrhoea with all the discomforts associated with this condition, but both also suffered bone pains and progressive kyphosis, characteristic of osteomalacia and confirmed by bone biopsy. In the one case, a number of spontaneous fractures occurred. Feeling that the osteomalacia was probably associated with the steatorrhoea, and that this latter might result from, or be accentuated by, the small reservoir and the presence of an afferent loop, conversion to a Billroth I gastrectomy, with a Henley loop, and vagotomy was carried out in each case. The results were disappointing since, although the dyspeptic symptoms were improved, the steatorrhoea and symptoms of osteomalacia have been unaffected.

Milder degrees of steatorrhoea can be helped as described in Chapter 10. The type that leads to severe malnutrition and considerable discomfort but without osteomalacia, is best treated by conversion of the gastro-jejunostomy to a gastro-duodenostomy; where the stomach reservoir is small, or where there may be tension on the anastomosis because of the small stomach, a loop of jejunum or transverse colon can be interposed. This usually reduces fat loss, cures the diarrhoea and leads to a general improvement in health.

This chapter has so far covered the various troubles which may continue beyond the first few months and which, therefore, have to be accepted as something of more than a temporary nature. I have classified them under causative factors, and each one of these, if acting alone, leads to a fairly precise pattern of discomfort.

Another fairly clear-cut pattern of post-gastrectomy discomfort, but coming on after an interval of satisfactory health, is the so-called 'afferent loop syndrome'. It might have been included, therefore, in the 'delayed' group of complications, but is described here because of its moderately precise features, and also because it may be associated with alteration of fat metabolism as revealed by increased fat in the stools. Usually it is not so serious or dramatic as the 'sumping' described above.

Afferent Loop Syndrome

The chief features of the 'afferent loop syndrome' are the development of an increasingly distressing feeling of fullness soon after meals, which at first, may pass off spontaneously, but which before long is only relieved by vomiting, this consisting of pure bile varying in amount up to 200–300 ml. Less commonly, the vomit consists of undigested food heavily mixed with bile. The pure bile element suggests temporary obstruction of the afferent loop followed by sudden relief; the food-plus-bile type of vomit points to a passing obstruction of the efferent loop either at the stoma or just distal to it, and since vomiting does not occur every time food is taken, the obstruction is intermittent. Mimpriss and Birt (1948), and others, have hinted at some mechanical explanation, such as that, for some reason, the afferent loop becomes obstructed as bile and pancreatic secretions pour into it, and then, as a result of some movement of the body or extra powerful peristalsis, it becomes unblocked with resulting filling of the stomach with these irritating fluids, and consequent vomiting. Steinberg (1954) and Wells and Welbourn (1951) suggested that this obstruction resulted from adhesions gradually developing at the point where the afferent loop joins the stomach—this usually being on the lesser curve side—and that these caused some kinking of the loop.

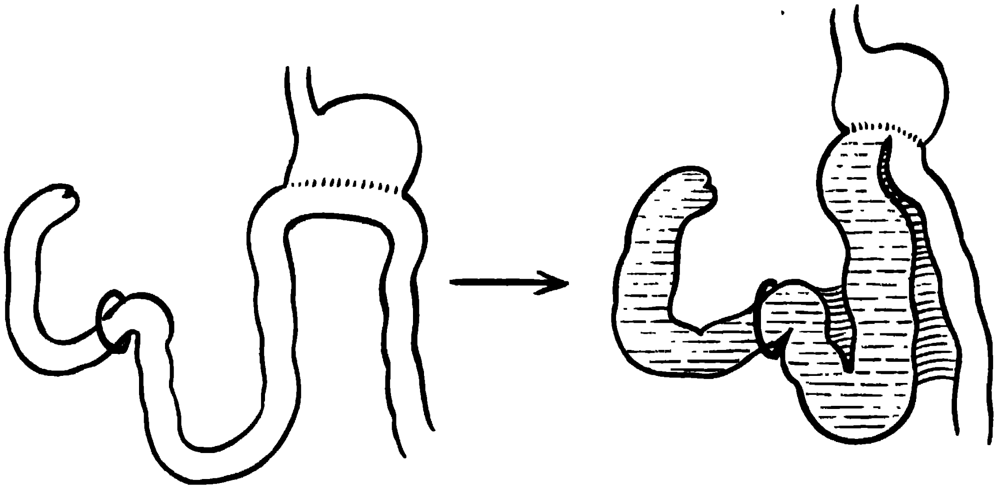

Figure 19. The genesis of afferent loop embarrassments

When the loop is fairly suddenly filled with bile and pancreatic secretions the kinking becomes exaggerated, amounting to real obstruction (*Figures 19* and *20*). The distended afferent loop may, at the same time, press on to the efferent loop, causing some degree of obstruction. Certain features of 'dumping' are sometimes superimposed on to the afferent loop syndrome. As pointed out by Taylor (1959), distension or stretching of any part of the upper small intestine, whether by balloon or by a weighted bag, produces these dumping symptoms and, of course, this applies equally to afferent or efferent loop. Because of the temporary obstruction in the afferent loop syndrome, lying down does not generally relieve it, although when it does it is probably because it allows the distended, heavy and dependent loop to become unkinked. 'Dumping', on the other hand, is more usually associated with distension of the efferent loop, and this is not accompanied by any obstructive factor. Dumping, therefore, is relieved by assuming the recumbent position, since this compensates for the accompanying hypotension already described. Taylor also points out that where any doubt exists as to whether dumping is caused by afferent or efferent loop, one can usually differentiate by the fact that if large meals and sugar are avoided, the patient can escape the dumping symptoms of efferent loop origin but not the distension symptoms due to

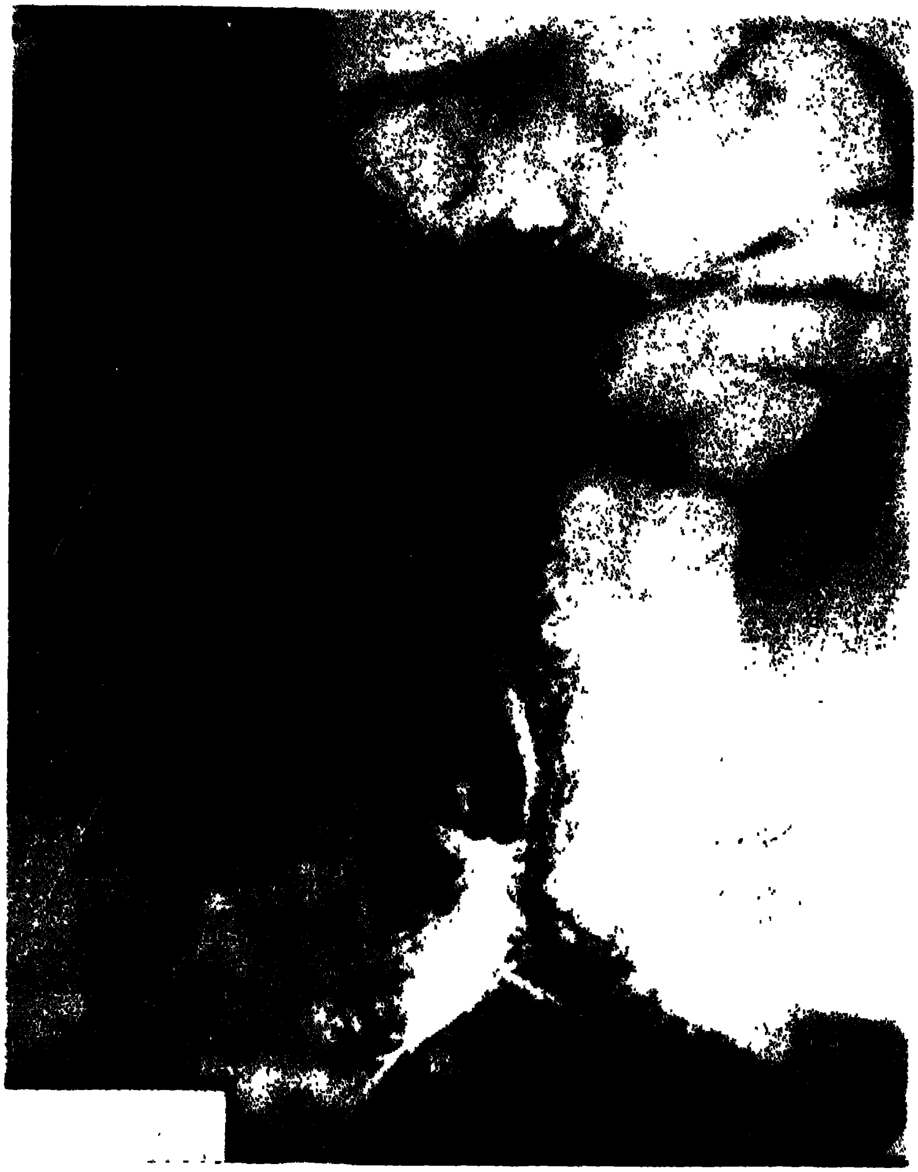

Figure 20. Afferent loop syndrome

obstruction of the afferent loop. I subscribe to his hypothesis that when the vomit consists of food as well as of bile, this points to intermittent obstruction of the efferent pathway, probably by compression by the adjacent distended afferent loop to which the efferent loop is adherent. Another possible explanation is that should rotation of the anastomosis be present, as described under 'immediate post-operative complications', and should the afferent loop become slowly distended, as in the afferent loop syndrome, this, by contiguity, may exaggerate the rotation and embarrass the efferent loop.

Incidentally, when exposed, the mechanical factors embarrassing the afferent and efferent loops may not at first be apparent, but if there is air in the stomach, compression of this will fill the afferent loop and show up the effects of adhesions; should the stomach be empty, the anaesthetist can inject air or saline through the Ryle's tube.

As already mentioned, some patients with an over-long or enlarging afferent loop develop increased frequency of bowel actions; this, on investigation, may be found to be associated with an increase in fat excretion, though usually of mild degree, e.g. up to 8–10 g/day, and not accompanied by the features of full-blown steatorrhoea. This can be understood since pancreatico-cibal asynchrony is certainly caused by the same mechanisms.

The afferent loop syndrome, being of mechanical origin, obviously needs a surgical procedure to correct it, and several operations are available. Effective drainage of the afferent loop may be achieved (*a*) by detaching it from the stomach and joining the end on to the side of the efferent, in the manner of a Roux-en-Y anastomosis; (*b*) by performing a side-to-side entero-enterostomy just distal to the original gastro-jejunostomy stoma; or (*c*) by a wider junction extending right up to the stomach—the so-called 'pantaloon' operation described by Steinberg (1954) and Wells and Welbourn (1951).

Each of these operations diverts the alkaline duodenal contents from the gastro-jejunal stoma and so exposes ulcer-susceptible jejunal mucosa to the digestive action of the remaining gastric secretions. After these procedures, therefore, there is a high risk of jejunal ulceration which is largely mitigated by adding vagotomy. I have used the Roux-en-Y anastomosis plus vagotomy, a technique which I have employed in three patients with afferent-loop syndrome, all of whom have responded satisfactorily. Nevertheless today I would convert to a Billroth I type reconstruction plus vagotomy.

A variant of the anatomy usually associated with the afferent loop syndrome sometimes results from an extra long loop, e.g. 30–

45 cm. The majority of patients who have long afferent loops have no trouble of this kind, but occasionally the loop assumes a concertina'd pattern as a result of becoming wrapped in adhesions (*Figure 21*). The symptoms are similar to those described above and result from retention of secretions with consequent distension and pain. I have had six such cases, five following ante-colic operations and one following a retro-colic operation. It cannot be stressed too often that with retro-colic anastomosis there should be no afferent loop at all. A retro-colic afferent loop lies in a crowded position to the left of the vertebral column and beneath the transverse colon and meso-colon. The D.J. junction is fixed but beyond this point the jejunum is normally free. With gastro-jejunostomy, however, it is also fixed at the stoma, and this second fixation is augmented by the fact that the edges of the meso-colon are stitched to the stomach stump. This crowding and fixation tends to encourage adhesion formation, and concertina'ing of the loop (see *Figure 7*). One method of treatment is to excise the redundant loop and to reconstruct by a Roux-en-Y anastomosis, as advocated for the more usual form of afferent loop syndrome. The alternative, which is less disturbing physiologically, is to convert to a gastro-duodenostomy, and to add vagotomy.

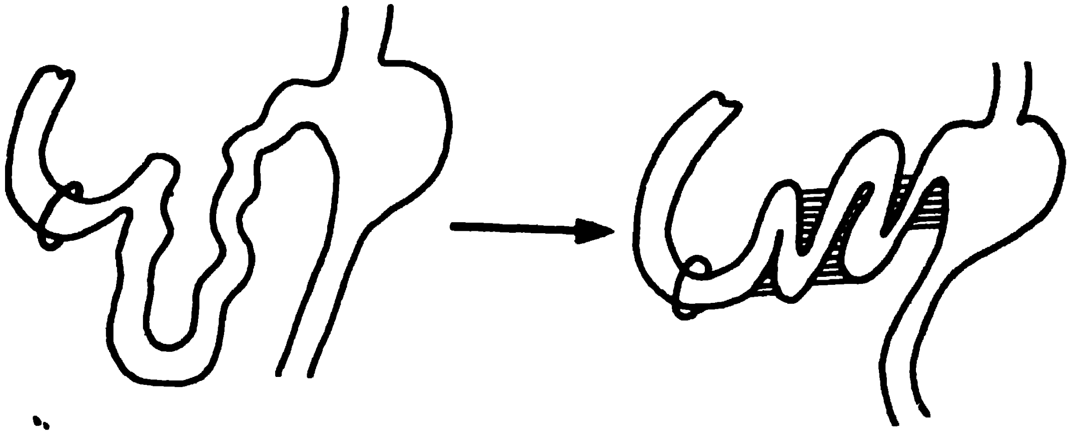

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Figure 21. Concertina'd afferent loop

However many cases of post-gastrectomy syndromes one sees, it always seems possible to meet with yet another kind of afferent loop complication, and the following is an interesting example.

A man, now aged 45, had had a partial gastrectomy elsewhere in 1947. He was well until 1951, when he developed attacks of diarrhoea, the stools being bulky, pale and offensive, and in the course of the next few years he lost 3½ stone in weight. Latterly, the diarrhoea interfered with his activities and gave him a feeling of insecurity—indeed, on occasions following a particularly bulky stool he fainted; he also experienced abdominal pain from time to time. X-ray of a barium meal revealed an enormous afferent loop and appearances in the small intestine characteristic of steatorrhoea (*Figures 22* and *23*). He was not anaemic and the serum vitamin B_{12} level was normal, but the faecal fat content over ten days averaged 12·8 g/day. On 29.3.62 the abdomen was opened by a transverse incision. The stomach and anastomosis were adherent to the anterior abdominal wall, and other dense adhesions were encountered. Approximately half the stomach had been removed at the first operation, and the anastomosis was ante-colic, afferent-loop-to-greater-curve (Moynihan). The afferent loop itself was not less than 60 cm in length, and the part attached to the stomach was very widely dilated—indeed, it was as big as the stomach stump itself. The efferent loop was hypertrophied and wider than normal. Adhesions were found where the afferent and efferent loops hung down from the stomach, thus maintaining a kink at each of these points. All these observations suggested that the steatorrhoea was due to the very long afferent loop. The dilatation of the jejunum opposite the full-width stoma probably resulted from an element of obstruction caused by the adhesions and, possibly, some degree of atonia. Before opening the bowel needle aspirates were taken. The viable counts from afferent and efferent loops were 1,200 million and 600 million organisms/ml, respectively, with an almost pure growth of *E. Coli.* After separating the adhesions the anastomosis was taken down, the dilated part of jejunum was excised, and the jejunum reconstructed by an end-to-end anastomosis. Gastric reconstruction was effected by conversion to a Billroth I form, and vagotomy was carried out. Apart from a mild pulmonary embolic incident, convalescence was satisfactory. The

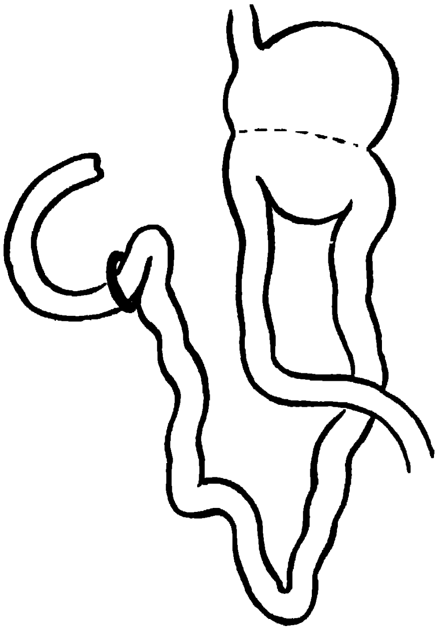


Figure 22. Moynihan type anastomosis with very long loop, that part opposite the stoma having become very dilated

Figure 23. Enormously dilated loop opposite stoma

average post-operative faecal fat over five days was 7 g/day, and his symptoms of diarrhoea and faintness cleared up. The latest report is that he has lost all his symptoms and has regained his confidence.

SUMMARY OF THE CLEAR-CUT POST-GASTRECTOMY SYNDROMES

The five relatively clear-cut post-gastrectomy syndromes discussed above are: little stomach reservoir; dumping; intestinal hurry; steatorrhoea; and the afferent loop syndrome. All have been described by various authors and all are generally accepted as distinct entities. However, since they occur relatively infrequently in a surgeon's experience, they may present difficult problems for analysis when encountered. This is especially so when presenting with a mixed pattern of complaints, resulting from more than one anatomical or physiological factor being operative at the same time. Nevertheless if, when faced with a puzzling set of symptoms, one keeps in mind the individual anatomical or physiological factor generally accepted as being associated with a specific pattern of complaints, one can often recognize elements of several of these factors, and so build up the whole picture under consideration.

Let us review the syndromes and relate them to their corresponding anatomical and physiological causes.

Small Stomach

A feeling of fullness early in the meal; inability to eat reasonably-sized meals; loss of weight and energy, even under a régime of six meals each day. However, it must not be forgotten that anaemia may cause mild degrees of the same discomforts.

Dumping

A feeling of weakness and dizziness immediately after a meal, accompanied by a sensation of heat or cold associated with a strong urge to lie down; sometimes even loss of consciousness. This pattern of symptoms is related to the rapid delivery of undigested hypertonic food into the efferent loop. A small reservoir probably aggravates this, although it should be remembered that once the antrum and pylorus have been removed, food leaves the stomach continuously no matter how large the remaining reservoir. The different factors, distension, hypovolaemia and hypotension, all contribute.

Intestinal Hurry

Increased frequency of stools and a sensation of intestinal activity in the form of borborygmi or active gastro-colic reflex. This, again, is probably the sequel to a small stomach reservoir which, with no antrum or pylorus, delivers roughly masticated food into the jejunum as soon as it is swallowed, and so leads to increased peristalsis.

Steatorrhoea

The passage of pale, foul and bulky stools which float on water suggests steatorrhoea. It is usually accompanied by frequent stools but, occasionally, constipation. There are several factors responsible for fat malabsorption: (*a*) by placing food directly in the jejunum the normal stimulus for bile and pancreatic secretions is reduced, affecting both timing and quantity of enzymes (Butler, 1961); (*b*) the presence of an afferent loop impedes the onward flow of these secretions, interfering with their proper admixture with food. Obstruction of the afferent loop may increase with the passage of time; (*c*) the bacterial content of this relatively blind loop may play a part in inactivation of enzymes.

The Afferent Loop Syndrome

The development of a feeling of fullness during the latter part of a meal, not relieved by lying down, but often by vomiting up to 300 ml of pure bile; this syndrome is due to the afferent loop becoming involved by adhesions in such a manner than when filled rather rapidly by bile and pancreatic juices consequent on the stimulus of food, it becomes obstructed at the stoma. The afferent loop may become markedly distended, causing pain.

Mixed Syndromes

Regarding mixed syndromes, one can appreciate, therefore, that a patient who is a 'dumper' may also have intestinal hurry resulting from increased peristalsis. Another patient, suffering the symptoms of the afferent loop syndrome may, on investigation, be found to have raised faecal fat, a sequel to the pancreatic juices being retarded in their onward flow by the effect of the adhesions involving the loops. Again, the vomits of the same patient may consist of undigested food heavily mixed with bile, rather than of pure bile. This latter feature suggests some degree of obstruction on the efferent side of the stoma, or of the efferent loop itself just beyond the stoma, brought about by the pressure of the distended afferent loop on these parts. In a similar manner, as pointed out by Taylor, patients who are victims of these afferent loop embarrassments may also experience certain features of 'dumping'.

It is always important to assess the psychological stability or otherwise of any patient before advising operation. This is especially so in these post-gastrectomy problems. The delayed types are less likely to be functional; the clear-cut symptom complex is usually genuine; these mixed types are difficult.

There are other complications which come on much later, and after an intervening period of entirely satisfactory health. These will be considered under the heading 'delayed'.

DELAYED COMPLICATIONS

The discomforts referred to under this heading come on late, often several years after the original operation, during which good spell the patients may have been included in the 'cured' group. The new complaint may be pain not unlike the original ulcer pain and so the patient rather naturally assumes that it is a return of the old trouble. For instance, stomal ulcer usually declares itself as epigastric pain caused by food, although, on analysis, there are minor differences from the original ulcer pain. In many cases, the new discomfort is quite different from the old and is often of mechanical origin. In others, the patient merely feels generally out-of-sorts, lacking in energy and sometimes complains of a feeling of distension. The cause of such malaise may well be slowly developing metabolic changes, such as failing nutrition or anaemia, with or without vitamin B_{12} deficiency.

Stomal Ulcer

Often referred to as 'recurrent' ulcer, it is, of course, an entirely new one. The incidence of this complication, generally confined to instance, until recently, it appears to have been more common in the U.S.A. than in Great Britain.

The incidence in Birmingham is low, and Brookes, Waterhouse and Thorn (1960) could find only 15 cases out of 826 patients who had partial gastrectomy, which is less than 2 per cent. Balint and colleagues (1957), analysing 160 cases of anastomotic ulcer from three different hospitals, quote an incidence of 3–5 per cent following partial gastrectomy, and a somewhat higher one after simple gastro-enterostomy.

Goligher, Moir and Wrigley (1956), in an investigation comparing the results of 132 Billroth I and 138 Billroth II operations for duodenal ulcer, report a stomal ulcer rate of 15·1 per cent and 1·5 per cent, respectively; in no operation was less than three-quarters of the stomach removed, but in none was vagotomy added. The time of onset of stomal ulcer varies; after gastrectomy it tends to occur within three years, although in Goligher's series the majority developed within 18–24 months; after simple gastro-enterostomy it develops considerably later. Hyperacidity and an increased volume of gastric secretion from the gastric remnant are presumed to be important aetiological factors, although in the presence of gastrojejunostomy it is difficult to collect the whole secretion; continuous suction with a mechanical pump will often help. Some believe that gastric peristalsis produces turbulence within the stoma, which may cause minor trauma to the mucosa, thus paving the way to ulceration.

During the past few years a number of American Centres, following the lead of Harkins, have been treating duodenal ulcer by antrectomy and vagotomy, and claim that the incidence of stomal ulcer during the first two years (the longest period at the time when the first reports were being discussed) is less than 1 per cent; this is rightly regarded as a great advance. At the meeting of the Southern Surgical Conference in Houston in 1960 I heard three series reported, the largest being 800 cases, and all three reports agreed on this low incidence of stomal ulceration.

The predominant symptom of stomal ulcer is pain usually brought on by food. The pain is usually felt more to the left than was the original ulcer pain, particularly when there is a gastro-jejunal anastomosis. Tenderness may be marked, often to the left of the midline, in fact, just where the anastomosis of a Billroth II gastrectomy usually lies. Following this type of gastrectomy, ulceration usually develops in the efferent loop on the jejunal side of the stoma. The ulcers may be multiple, in which event the afferent loop may also be affected. Following Billroth I gastrectomy, anastomotic ulcer usually develops on the gastric side of the stoma.

Bleeding in the form of haematemesis or melaena may occur, and not infrequently bleeding is the presenting symptom. In the absence of pain and where bleeding is gradual and persistent, the patient may seek help because of the more vague symptoms of anaemia; and it has to be remembered that one of the symptoms of anaemia is a feeling of distension hardly amounting to pain. Like the original ulcer, gastric or duodenal, these stomal ulcers may heal temporarily, only to recur. The resulting scar tissue tends to render the stoma somewhat rigid, and even to narrow it, leading to a degree of obstruction. This complication may also be intermittent, since the congestion and oedema associated with re-activation of the ulcer can aggravate this narrowing of the stoma. Anastomotic ulcer may perforate or, on the other hand, it may penetrate or cause a localized abscess. Depending on position, these ulcers may also become firmly adherent to colon, liver, pancreas or anterior abdominal wall.

Confirmation of a suspected anastomotic ulcer is often difficult since repeated x-ray examination may fail to reveal a crater. When positive, however, x-rays are of great value (*Figure 24*). On other occasions, the radiologist may comment on such variations from normal as a somewhat rigid stoma, or the presence of hypertrophic mucosal folds on the gastric side. Gastroscopy will sometimes help particularly with anastomotic ulceration after a Billroth I operation, but rarely reveals anything distal to the stoma of a Billroth II operation. The detection of occult blood, if not frank melaena or haematemesis, is strongly in favour of ulceration being the cause of the symptoms. On the other hand, excoriation of an area of gastritis or enteritis involving the region of the stoma may occasionally lead to occult bleeding. Such excoriation may heal or, in the presence of acid gastric secretion, may be the precursor of stomal ulceration.

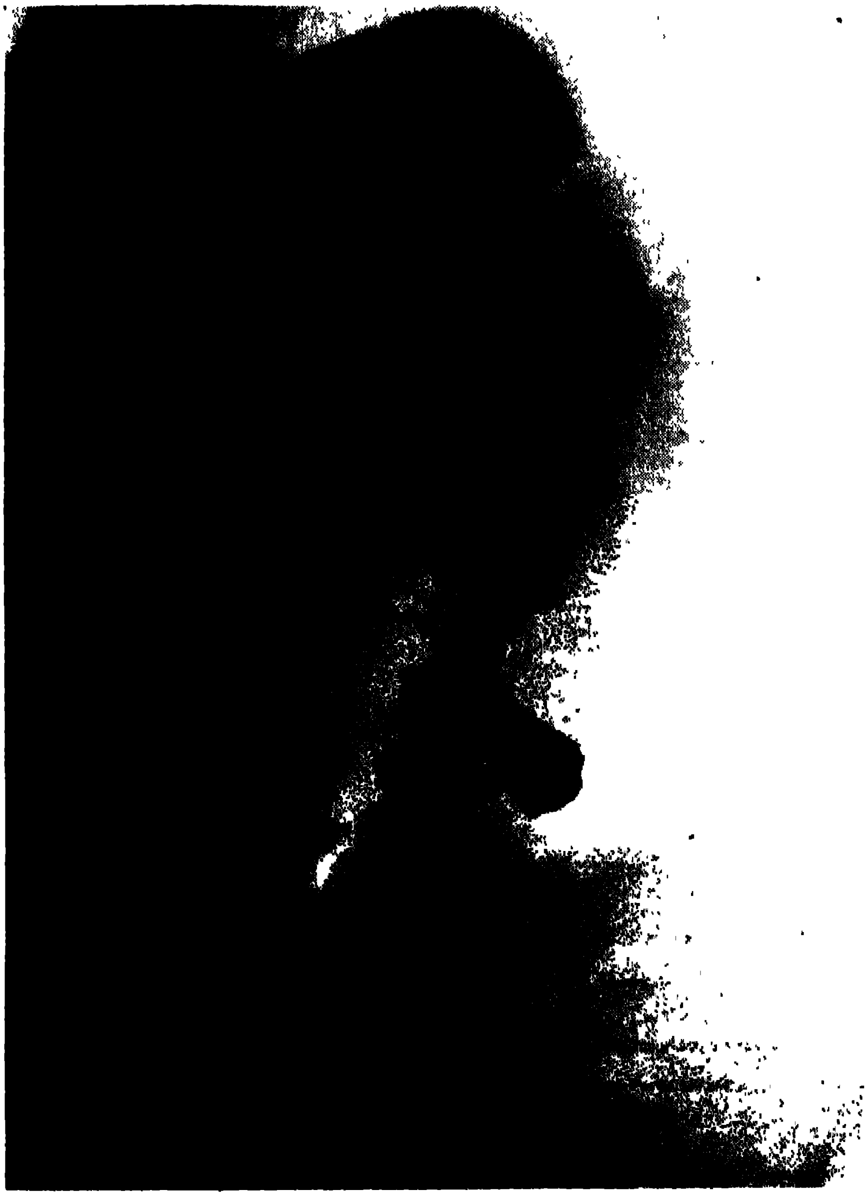


Figure 24. Stomal ulcer

When stomal ulceration is proved, medical treatment, including that for anaemia, is usually given a trial, and may succeed in keeping the patient comfortable for some time, although it tends to fail even more often than it does for the original duodenal or gastric ulcer. Operation should therefore be advised for radiologically-proved ulcers, or for recurrent bleeding where there is a highly suggestive history, even though the x-rays fail to show an ulcer or show only rigidity of the stoma or hypertrophic mucosal folds.

Because of technical difficulties the operation carries a higher mortality rate than does the original one for peptic ulcer, and these difficulties are even greater with a retro-colic anastomosis than with ante-colic reconstruction. Adhesions are often massive and their separation is accompanied by considerable bleeding and continued oozing. The ulcer can usually be seen or felt, but the area may be surrounded by gross inflammatory reaction. Some surgeons believe that vagotomy alone is sufficient to permit healing of the ulcer. I believe this to be true for the ulcer on the gastric side of a Billroth I gastrectomy for gastric ulcer, as also for the stomal ulcer developing fairly early, e.g. within 2 3 years of a Billroth II type operation for duodenal ulcer. However, where, after a Billroth II operation, the stomal ulcer has recurred several times, and according to x-ray appearances is accompanied by fibrosis and distortion of the stoma, vagotomy alone will not overcome this element of obstruction, and some form of reconstruction is indicated. For ulceration after a Billroth II type of operation I prefer to take down the anastomosis, to excise the ulcer-bearing part of the jejunal loop and to remove sufficient stomach to be rid of any scarred area and gross hypertrophic mucosa. I then prefer conversion to gastroduodenostomy accompanied by vagotomy, because I am satisfied that, being more physiologically normal, it gives better results than another gastro-jejunal reconstruction.

Most surgeons who have performed several hundred partial gastrectomies will have met with what might be termed the 'inveterate ulcerator'. By this term one refers to the patient who develops his first anastomotic ulcer soon after his original operation, and then in quick succession continues to produce new ulcers, even though more and more of the ulcer-bearing area has been removed on successive occasions until finally vagotomy is added. Eventually, so little stomach remains that the latest ulcer is near the cardia. Under such circumstances one is faced with the difficult decision as to whether to perform a total gastrectomy. Knowing the very high incidence of dyspeptic and metabolic crippling that follows this procedure, one is loath to remove the entire stomach.

In view of the increasing knowledge of the relationship between gastric secretion and non-beta cell tumours of the pancreas, as originally described by Zollinger and Ellison (1955), one's thoughts naturally turn to this possibility in such cases. It is therefore essential to investigate accordingly with special reference to nocturnal gastric secretion, pH and response to the augmented histamine test. In the presence of gastro-jejunostomy, collection of secretion is not easy, although one may get some indication of considerably larger volumes than usual and of lower pH. Summerskill (1959) pointed out that general hyperplasia of non-beta cells throughout the pancreas can cause similar effects. In cases of repeated recurrence of anastomotic ulcer associated with hypersecretion and raised acidity, it is therefore important to explore the pancreas for such a tumour; where none is found, it may be justifiable to remove the left half of the pancreas. I did this in one case, but there was no evidence of hyperplasia and it did not stop future ulceration.

Another line of investigation in these baffling and serious cases is suggested by Welbourn and Doggart (1956) who have shown the relationship of hyperparathyroidism to hypersecretion and duodenal ulcer. I have studied serum calcium and phosphorus levels and urinary calcium excretions in such cases but have not yet encountered a case of peptic ulceration in association with hyperparathyroidism. The following case illustrates the problem of inveterate ulceration where no evidence could be found of a Zollinger–Ellison tumour or other endocrine disorder.

L. S. was only 15 years old when he developed dyspepsia. He had his first operation in 1912 at the age of 25, and the history suggests that a perforation was sutured. In 1924 a retro-colic gastro-enterostomy was performed and he remained well for the next 22 years. Then, after five years of intermittent dyspepsia, a barium meal revealed an ulcer in the jejunum close to the stoma and also indicated some stenosis with delayed gastric emptying. Gastric acid studies showed a small overnight residual juice and a rapid acid response to a gruel meal. This was four years before the publication of the classic paper of Zollinger and Ellison (1955) but, in retrospect, the low resting gastric secretion was thought to make unlikely the diagnosis of such a tumour as they describe in their case. As a result of the radiological finding of a stomal ulcer a third operation was performed in May 1951, when ulcers were found in the duodenum and jejunum. A retro-colic three-quarters gastrectomy was performed and a Roux-en-Y anastomosis performed since the afferent loop was too short to bring up to the stomach. Unfortunately, at that time I did not appreciate the necessity of adding a vagotomy to this type of operation and within six months the stomal ulcer had recurred. At the fourth operation there were, once again, two ulcers, one on either side of the stoma. The ulcer in the jejunum had penetrated to, but not yet communicated with, the transverse colon and necessitated the removal of 12 cm of the colon. On this occasion, by mobilizing the D.J. junction, it was possible to convert to a standard retro-colic Billroth II type of operation, i.e. without an 'en-Y' anastomosis. A year later a third stomal ulcer had occurred, and at a fifth operation more of the stomach was removed and another Billroth II anastomosis performed, this time in front of the colon. At this laparotomy the pancreas was explored for evidence of a tumour but none was found. It must be stressed, however, that by this time adhesions and successive ulcers, having penetrated into the pancreas, made the exploration difficult. By now there was little of the body of the stomach left but its secretions proved sufficient to lead to a fourth stomal ulcer after 3½ years of freedom from symptoms. The last operation was performed in 1958 when he was aged 71. A trans-thoracic vagotomy led to complete relief of his pain, and three years later there was no radiological evidence of ulceration.

Gastro-colic Fistula

This condition is really a complication of stomal ulcer, particularly in the presence of a retro-colic gastro-jejunostomy or simple gastro-enterostomy. This association with retro-colic anastomosis is easy to understand, since the crowded position of structures under the meso-colon tends to bring such an ulcer into contact with the colon. In Lowdon's series of 46 patients (1953), 45 were cases where the original operation was for duodenal ulcer, and 39 followed retro-colic gastrectomies. The history usually begins, therefore, with symptoms suggestive of stomal ulcer, and then during a recurrent phase there occurs a fairly sudden onset of diarrhoea, occasionally with foul eructations and, rarely, with faecal vomiting. In the few cases that I have encountered, this diarrhoea has been marked and has led to malaise, rapid loss of weight, and is sometimes so sudden and severe as to result in serious fluid and electrolyte loss. The diarrhoea is due to the enteritis which follows contamination of the small intestine by colonic organisms. A barium meal may fail to show the fistula or even the stomal ulcer, although a barium enema in the same patient may demonstrate the fistula. The appearance of barium in the transverse colon within a few minutes of a barium meal strongly suggests the diagnosis, even though the actual site of the fistula is not defined (*Figure 25*). In the same way, a barium enema may show barium in the stomach. Because of the enteritis, there is much fat and fatty acids in the fluid stools. Flocculation of barium, typical of a malabsorption syndrome, is often shown on x-ray.

It is obvious that a gastro-colic fistula can only be cured by operation. Until a decade or so ago this was carried out in two stages, a proximal colostomy being the first one (Wilkie, 1934). Since the introduction of chemotherapy, and with sound methods of restoring fluid and electrolyte balance, it is now usual to operate in one stage (Lowdon, 1953). In a severely ill patient, however, it may be safer to use a staged procedure.

Having corrected water and salt depletion, the bowel is prepared by giving a poorly-absorbed sulphonamide or antibiotic. The operation consists of separating the colon from the anastomotic area, suturing the hole in the colon transversely and then dealing with the stomal ulcer by a further partial gastrectomy and vagotomy. If a massive inflammatory reaction is present making dissection hazardous, it is safer and more expeditious to resect the affected colon and gastro-jejunostomy *en bloc*, and then to re-suture the appropriate ends of intestine and to reconstruct by a fresh ante-colic

Figure 25. Gastro-colic fistula

Billroth II type gastrectomy or conversion to a Billroth I gastrectomy, adding vagotomy. Excellent accounts of gastro-colic fistula are given by Lowdon (1953) and by Rosenqvist and Sjoberg (1954). The following is a typical case.

In 1946 A. O., a man aged 44, was treated elsewhere for pyloric stenosis by gastro-enterostomy. He remained well for five years, and then developed right-sided abdominal pain one hour after meals. In February 1953 he was admitted to the Queen Elizabeth Hospital because he had developed diarrhoea with 4-5 stools each day and foul eructations. The stools also were offensive, pale and floated on water. He had lost weight, suffered severe bronchitis and had oedema of the ankles. Barium meal revealed a gastro-colic fistula. Because of his nutritional state and bronchitis, it was five weeks before he was fit for operation. After preparation with phthalyl-sulphathiazole he was operated on and the area of the fistula was explored. The stomal ulcer was on the anastomotic line opposite the efferent loop, so that both stomach and jejunum communicated with the transverse colon. With clamps on the colon the whole area of the ulcer was excised. Both colon and jejunum were sutured in continuity, and after removing three-quarters of the stomach the fundus was anastomozed to the second part of duodenum (Billroth I). Vagotomy was added. His convalescence was uneventful.

In January 1962 he was admitted with an incisional hernia which had become more troublesome since he had put on weight. He was completely free from all gastro-intestinal symptoms.

Obstruction-en-Coccoon—Efferent Loop

This is an interesting form of delayed complication resulting from partial obstruction of the efferent loop just beyond the stoma. It presents with such constant features as to amount, almost, to a separate post-gastrectomy syndrome. The alternative term 'efferent loop syndrome', however, might be misleading, since this could be thought to include the 'dumping syndrome', so much of which is due to distension of the efferent loop.

I have encountered eight such cases in the past ten years, and surgeons from other hospitals have told me of similar experiences. All were following a retro-colic partial gastrectomy, and all patients had enjoyed several years of good health before developing a feeling of fullness soon after meals. This symptom fairly rapidly became worse and was soon accompanied by vomiting. The early discomfort soon amounted to pain, sometimes of a colicky nature, which was relieved only by vomiting. The vomit always contained recently-taken food. There was fairly rapid weight loss, the patients felt weak and usually lost time from work. Sometimes the patient felt faint and dizzy and he perspired, probably due to distension of the efferent loop. Two patients volunteered the statement that sometimes they could see a swelling just to the left of the midline, and in one witnessed this myself. These features pointed to sub-acute high intestinal obstruction, almost certainly involving the efferent loop, and x-ray studies sometimes confirmed this. In each case the operative findings were precisely the same, i.e. a distended convoluted efferent loop involving anything up to 30–40 cm of the upper jejunum, and held in this position by a sheath of translucent adhesions (*Figure 26*). As with afferent loop abnormalities, the appearance on exposure may not at first be convincing, but if the stomach is squeezed to force air into the jejunum, the special configuration of the efferent loop will at once become apparent. The explanation of its genesis is not clear, but crowding to the left of the vertebral column may play a part.

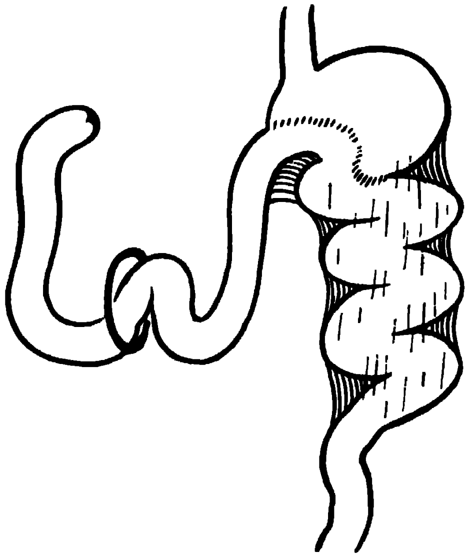


Figure 26. Obstruction-en-coccoon

It is a potentially dangerous condition, and one of our early patients died while we were trying to make up our minds as to his condition; nothing had been written on the subject up to that time.

Excision of the distended and chronically obstructed loop appears to be called for; my current practice is to convert the original Billroth II gastrectomy to a Billroth I operation, adding vagotomy.

Obstruction by a Food Bolus

Obstruction of the small intestine by semi-solid boluses of food in patients having had a partial gastrectomy is a rare occurrence.

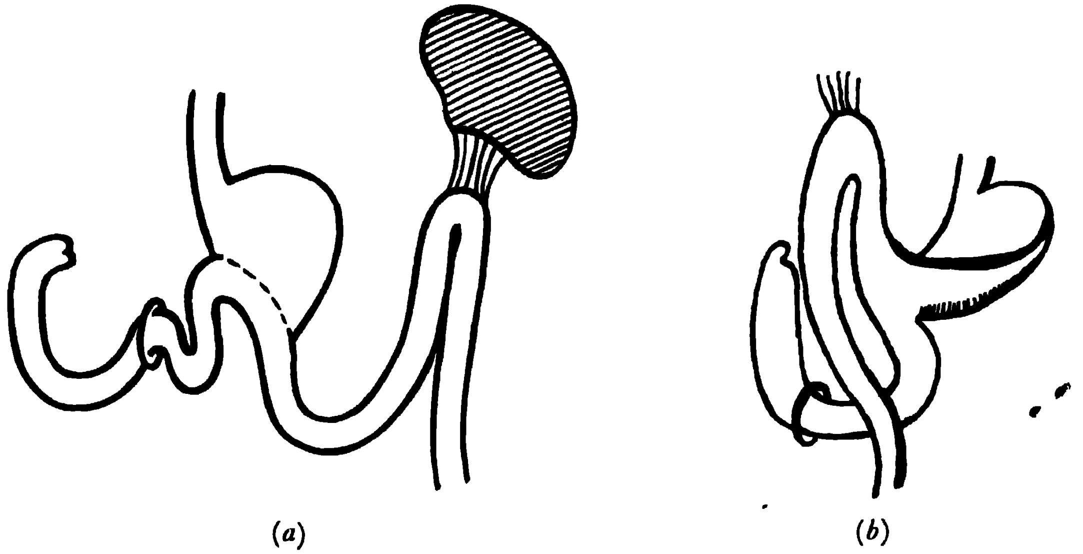
Nevertheless, when reports appear, such as those of Ward-McQuaid (1950) and Rains (1956) they are usually followed by a number of letters referring to similar isolated cases. Two patients admitted to the Surgical Professorial Unit with this complication were both found to be obstructed by a mass of undigested orange pulp. One obstructing mass, when removed, so resembled an intact orange that it was difficult to believe the patient's assertion that he had not swallowed the fruit whole. Undeterred by one such attack, the second patient was later admitted with a second orange pulp obstruction. At laparotomy on this second occasion it was possible to milk the obstructing pulp onward into the caecum without having to perform an enterotomy.

Orange pulp seems to be the most common obstructing agent, although others have encountered cases of obstruction due to nuts or banana. The essential feature of the original operation which pre-disposes to this complication is the removal of the antrum and pyloric mechanism. The antrum is normally responsible for the homogenization of the ingested food masses before they pass the pylorus; once the antrum is removed the only important site for the breakdown of large lumps of food is the mouth. It is therefore important, after partial gastrectomy, that the patient has adequate teeth or dentures and realizes the importance of thorough mastication. He should be warned of the dangers of bolting lumps of fibrous food.

The physical signs of bolus obstruction are similar to those characteristic of so-called 'gallstone ileus', the word 'ileus' being an inaccurate term, since colicky pain of sudden onset followed by progressively severe vomiting is the usual mode of onset. Bowel sounds are exaggerated, and the bowels may be moved once or more until the large bowel is empty. There is usually no tenderness in the abdomen. X-ray studies reveal small bowel obstruction. Such a picture in a patient who has had a partial gastrectomy should suggest the correct diagnosis. The suspicion is often confirmed by the patient's admission of swallowing the culpable food. However, the picture may be different, as in the following case. A colleague of mine had a patient with similar colicky pain but minimal vomiting, and at operation the food bolus was found to be in the blind duodenal stump, and on further examination was, in fact, discovered to be in a diverticulum of the second part of the duodenum which had not been noticed during the original operation. Once re-hydration and gastric suction have rendered the patient fit for it, treatment of an established obstruction is by operation. The obstructing mass can readily be palpated, and if it cannot easily be milked onward into the large bowel, enterotomy is required. It is wise to look for further undigested masses of food in the proximal bowel once this is decompressed. After operation the patient should be told how and why he became obstructed so that he may avoid a repetition.

Other Efferent Loop Obstructions

A solitary kink of an efferent loop due to an adhesion is a rare complication and I have seen only two such cases; yet in each one the radiologist was able to diagnose the condition. The history was similar in both patients, i.e. that partial gastrectomy of the ante-colic gastro-jejunostomy type had resulted in several years of complete comfort, and then, within a few weeks, fullness after meals and vomiting developed. In each case x-rays showed that the efferent loop, some 15–20 cm from the stoma, was acutely kinked and partially obstructed, in one case being tethered to the region of the spleen, and in the other to the under surface of the right lobe of the liver (*Figure 27*). The operations presented no difficulty and consisted of freeing the tethered loop. The onset of this complication is not unlike that of obstruction-en-coccoon, but in the latter the pain seems to be more intense, possibly because of the crowded position of the concertina'd coils of small bowel in the retro-colic positions.



[(*b*) Reproduced by courtesy of the Editor of *Birmingham Medical Review*

Figure 27. (*a*) *Efferent loop hooked up to spleen by adhesions;* (*b*) *another form of embarrassment of efferent loop by adhesions*

Jejuno-gastric Intussusception

This is one of the rarer complications, and one more likely to be found after simple gastro-enterostomy than after partial gastrectomy. It may develop during the immediate post-operative period or many years later. The onset is usually sudden, with colicky pain and vomiting. The vomit often contains blood and, in about one-third of the cases, a mass can be felt in the left hypochondrium. Gastroscopy may reveal the intussuscepted jejunum, and a barium meal will show obstruction at the stoma and possibly a filling defect in the stomach reservoir. It is nearly always the efferent loop that is involved, although cases have been reported of the afferent loop intussuscepting into the stomach. The condition may be recurrent and also self-reducing. Treatment is by operation; when the stoma is exposed, it may be possible to reduce the intussusception, but occasionally it is necessary to excise the parts involved because of irreducibility or gangrene of the intussuscepted jejunum. Smith (1955) published a case of his own and collected 16 more from the literature, and his paper gives an excellent summary of the problem.

Loss of Weight and Energy—Malabsorption and Malnutrition

Most reports on large series stress the high proportion of patients who, although otherwise comfortable, do not attain the ideal weight for height, age and sex, following partial gastrectomy. This is dealt with in more detail in Chapter 10, including devices for helping these patients.

Muir (1949), Brain (1953), Wells and Welbourn (1951), and many others since then, have given figures which indicate a high incidence of loss of weight after partial gastrectomy. It should be pointed out, however, that in most of these series the gastrectomies described were 'sub-total', in which 75–90 per cent of the stomach was removed.

Anaemia

This is covered fully in Chapter 8. The striking fact is that about 50 per cent of patients develop anaemia after the passage of a few years. A second point of importance is how vaguely the condition may declare itself—less energy, perhaps amounting to early fatigue, loss of interest in affairs, poor appetite, and sometimes a feeling of distension. In the absence of true gastro-intestinal symptoms, many months or even years may pass before the patient seeks advice. A simple solution is to keep all partial gastrectomy patients on iron, and this is stressed in our concluding remarks. The rare complication of sub-acute combined degeneration of the cord is also dealt with in Chapter 8.

Pulmonary Tuberculosis

A few years ago clinicians began to suspect that partial gastrectomy pre-disposed to the development of pulmonary tuberculosis, and the papers of Forsgren (1947), Isorni and colleagues (1948), Allison (1955) and others, suggested that the incidence was many times greater than in the average population.

It so happened that in the early 1950s, because there was a suspicion in Birmingham that there was a higher incidence of pulmonary tuberculosis amongst nurses than in the average population, it was decided that all admissions to the Surgical Unit should have routine pre-operative chest x-rays to see how many had unsuspected pulmonary disease. The timing of this was such that some 84 per cent of our peptic ulcer cases admitted during the five-year period 1950-54 had had pre-operative x-rays, and this afforded an excellent opportunity of finding out the incidence of the development of pulmonary tubercle in well over 800 cases of partial gastrectomy. Thorn, Brookes and Waterhouse (1956) undertook this enquiry.

Of the 800 patients x-rayed before operation, 60 showed old pulmonary tuberculosis lesions, 8 having a positive sputum at the time. Of those who developed active tuberculosis after operation, 5 women and 16 men came from this group of 60 with positive x-rays. In addition, 14 men with negative pre-operative x-rays subsequently developed active tuberculosis as did a further 4 in whom no pre-operative x-ray had been taken. Of the 60 with positive pre-operative x-rays, therefore, 21 had either been worsened or became freshly active, and 14 developed pulmonary tuberculosis without pre-operative evidence of lung disease. A further analysis is of great significance; the tendency to develop exacerbation or fresh infection does not depend upon the extent of gastric resection, nor upon the type of reconstruction nor, indeed, on the mere incident of operation, but on pre-operative state of nutrition. This probably accounts for the fact that gastric ulcer victims are more liable to develop tuberculosis than those of duodenal ulcer, since gastric ulcer is more common in under-nourished patients.

The most vulnerable type of patient is the under-nourished elderly man with high gastric ulcer. Thorn, Brookes and Waterhouse concluded that, at the time of their series, men with normal x-ray films of the chest who were less than 85 per cent of their standard weight prior to operation, were about fourteen times more likely to develop pulmonary tuberculosis after operation than those of normal weight. Today, with lower incidence of pulmonary tuberculosis and the newer anti-tuberculous drugs, the position is less serious. However, certain precautions are still indicated:

(1) All patients should have x-ray examination of the chest before gastric operations.
(2) A patient who warrants operation for a peptic ulcer, but who has active pulmonary tuberculosis or who has quiescent tuberculosis, and is under-weight and under-nourished, should first have anti-tuberculosis treatment and his nutritional state should be improved.
(3) For patients with active or old pulmonary tuberculosis, the preferred operation for peptic ulcer is one which will least damage their nutritional state. A vagotomy plus drainage procedure should always be considered rather than a gastric resection.
(4) A regular chest x-ray follow-up is indicated in patients with pulmonary tuberculosis who undergo gastric operations.

SUMMARY

So long as reconstruction by gastro-jejunostomy is employed, thus producing an afferent loop and, incidentally, by-passing the duodenum, it is difficult to know how to avoid many of the delayed complications of mechanical origin just described. For example, kinking of the loops at the stoma by adhesions, or concertina'ing of an over-long afferent loop, again by adhesions, both leading to the afferent loop syndrome, result from the new anatomy created by the operation. The same applies to slow dilatation of the afferent loop leading to steatorrhoea, and also to the development of obstruction-en-coccoon involving the efferent loop. It is certain that an ante-colic afferent loop should never be more than about 10 cm long, and a retro-colic anastomosis should abut on to the D.J. junction so that there is virtually no afferent loop at all. It will also be seen from the chapters dealing with altered metabolism that the afferent loop and incidental by-passing of the duodenum play a major part. All these post-gastrectomy complications can be greatly improved—often cured—by conversion to a Billroth I type of reconstruction plus vagotomy.

The cause of stomal ulcer is not yet fully understood. Inadequate reduction of acid and pepsin is clearly the predominant cause, but such ulceration may occur even when these factors are absent.

It may be that the protective mucin is deficient, but it could also be due to some endocrine activity. Zollinger and Ellison (1955) and Summerskill (1959), have shown that the pancreas may be responsible, and Hellström (1959) and Welbourn and Doggart (1956) have shown that hyperparathyroidism sometimes leads to ulceration. Cortisone therapy and pituitary hyperactivity are known to lead to ulceration. We need to know much more about these relationships.

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5

THE PHYSIOLOGY OF THE UPPER GASTRO-INTESTINAL TRACT

John A. Williams

> 'Some have made the stomach a mill; some would have it to be a stewing-pot; and some a wort-trough; yet all the while, one would have thought that it must have been very evident, that the stomach was neither a mill, nor a stewing-pot nor a wort-trough, not anything but a stomach.'
>
> *William Hunter*, 1784

The object of the surgical treatment of peptic ulceration is to reduce the acid pepsin secretion in the stomach. In achieving this object the operations in common use inevitably affect other functions of the stomach and small bowel. Following these operations the physiology of the upper gastro-intestinal tract is always altered to a greater or lesser extent and the following chapters will be devoted to a consideration of this altered function and its clinical and sub-clinical repercussions on the patient. There is considerable variation in the consequences of this alteration of the physiological state; at one extreme the patient who enjoys uninterrupted good health after the operation and, at the other, the patient who has 'never been the same since'. It will be seen that some alteration in physiological status follows every operation for peptic ulcer, and that most patients sooner or later develop some detectable abnormality. However, the symptoms and signs produced depend upon such varied factors as the sensibility or fortitude of the patient, the pre-operative body stores of minerals and vitamins and the metabolic needs of the individual concerned.

Before considering the effects of operations on the upper gastro-intestinal tract we must attempt to understand the normal physiology of the organs primarily affected by these operations: the stomach, the duodenum—together with the glands draining into it—and the jejunum.

The following is a short and very simplified account of the physiology of the upper gastro-intestinal tract. Simplification of a complex subject necessarily sacrifices precision. For a fuller description of the physiology the reader is referred to some of the many excellent monographs on the subject (Ivy, Grossman and Bachrach, 1950; James, 1957; Davenport, 1961; Gregory, 1962; and others).

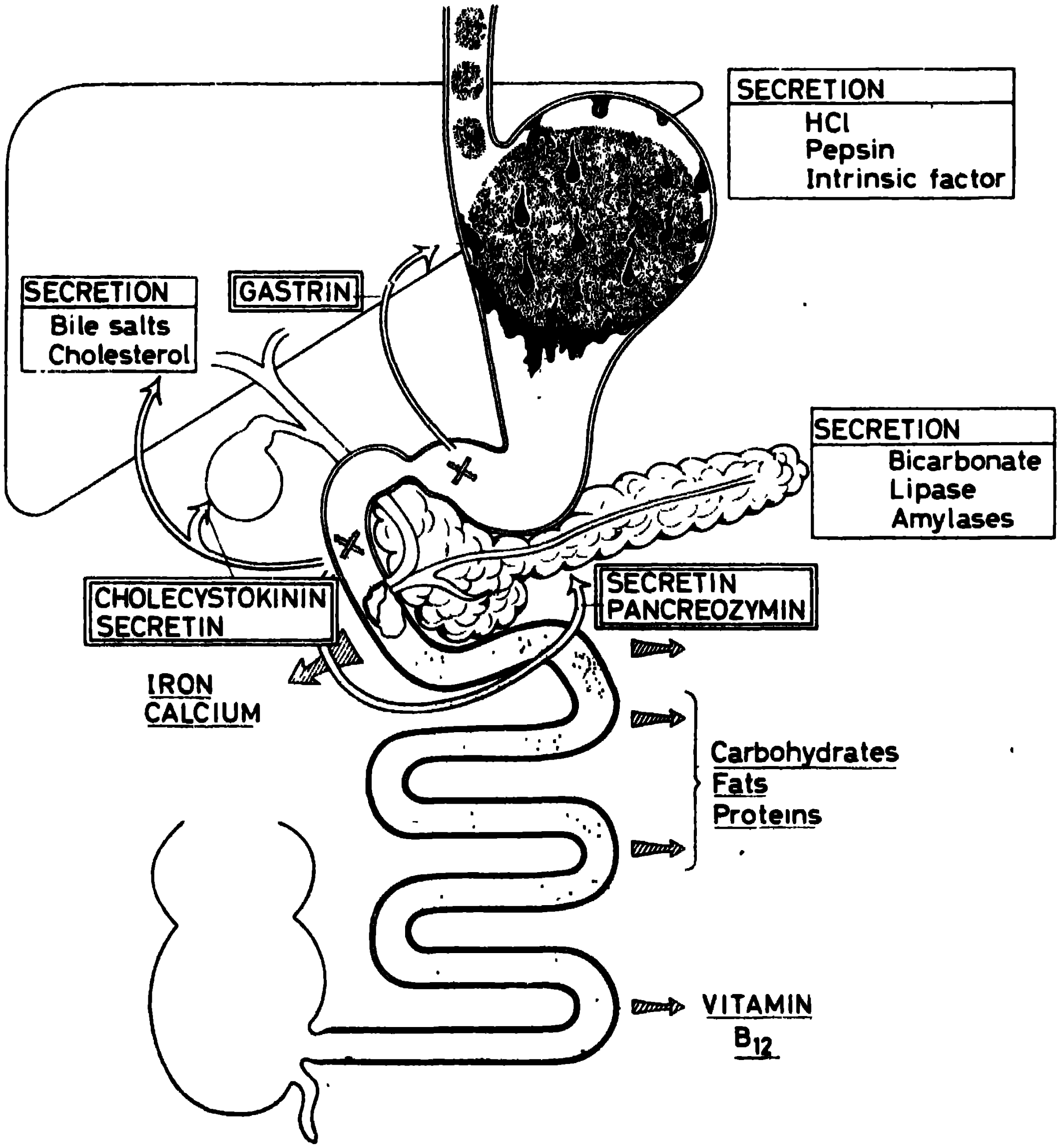

Figure 28. Diagram summarizing some of the important physiological functions of the upper alimentary tract

The processes of food preparation and digestion begin in the mouth with mastication and the production of saliva. However, these will not be considered here, since the physiological disturbances resulting from operation are almost entirely confined to that part of the alimentary tract below the diaphragm (*Figure 28*).

TABLE 5

	Function	*Digestion*			*Absorption*
		Carbohydrates	*Proteins*	*Fats*	*Minerals and vitamins*
Stomach	Storage. Homogenization. Sterilization. Periodic dispensing.	Continued salivary digestion. Up to 50 per cent digested.	Little digestion. Major effect is breakdown of cellular barriers.	Little or none. Fats are not emulsified.	Little absorption of water-soluble solutes. Alcohol is absorbed.
Duodenum with bile and pancreatic juice	Neutralization of acid. Emulsification of fats. Beginning of digestion.	50 per cent digested and absorbed.	50 per cent digested and absorbed.	50 per cent digested and absorbed.	Iron. Calcium.
Jejunum	Mixing of food and digestive juices by segmentation. Absorption.	Up to 100 per cent digested and absorbed.	80 per cent digested and absorbed.	Up to 100 per cent digested and absorbed.	Folic acid.
Ileum	Further digestion and absorption.	90–100 per cent absorbed.			Vitamin B_{12}.

STOMACH

The main function of the stomach is to process the ingested food into a form suitable for digestion, and then to dispense it in amounts small enough to permit optimal digestion and absorption in the small bowel. According to James (1957) the purpose of the stomach is to protect that most delicate and sensitive organ of the gastro-intestinal tract, the small gut. The stomach receives, edits and occasionally rejects ingested material which might injure the intestine. This ingested material may be hot or cold, dry or fluid, hyper- or hypo-tonic, and yet the boluses ejected through the pylorus are relatively constant in temperature, homogeneity and tonicity.

Homogenization

The breakdown of swallowed lumps of food in the stomach is brought about by two mechanisms working together, the churning effect of antral movements and the digestive action of gastric secretions. The first conception of the antrum acting like the gizzard of birds was proposed by Borelli (1680) but, even in birds, the breakdown of meat boluses was soon shown to be independent of the grinding action of the gizzard. Reaumur (1752) observed that meat placed in a perforated metal canister within the stomach of the kite underwent digestion and breakdown even though it was protected from the mechanical effect of grinding in the gizzard. As Hunter said, it is incorrect to liken the antrum to a mill, for there is no actual grinding as there is in the gizzard of the bird. It is rather better to liken it to the action of the modern washing machine. Food is churned about in the acid gastric juice just as washing is in the detergent solution in a washer; with food, as with washing, it is the combined effects of the mechanical and chemical factors which produce the desired results.

Mechanical

The mechanical function of the stomach is different in its upper and lower halves; this distinction does not correspond exactly with the anatomical divisions of the stomach, but can conveniently be referred to as the body (including the fundus) and the antrum. Mechanically, the body is primarily a distensible bag for the reception of food, whilst the antrum is the part in which vigorous peristalsis and mixing occur.

Solid or semi-solid food, masticated and mixed with saliva, is stored in layers in the distensible body where it is relatively undisturbed by peristaltic activity. The body secretes acid and pepsin which flow around the stored mass into the antrum. Similarly, swallowed fluids trickle past the food mass rather than being stored in layers, so that a drink taken at the end of a meal may pass the pylorus before the solids eaten. The food mass in the body of the stomach is therefore undergoing salivary digestion in its centre, whilst at the periphery the low pH of the gastric juice inactivates the salivary amylase and allows peptic digestion to begin. In addition to this peripheral bathing with acid and pepsin, the distal end of the food mass is gradually passed into the antrum where it is mixed thoroughly with the acid and pepsin secreted by the body. Here, waves of contraction pass regularly down towards the duodenum, not completely dividing off the antrum so that a pressure gradient is created, but mixing and helping to break up the food particles.

Chemical

The mechanical homogenization in the normal person is supplemented by the action of acid and pepsin which act by breaking down the tough cellular components of animal and vegetable food. Thus a combination of mechanical, physical and enzymatic mechanisms leads to the breakdown of rough food particles with the result that the boluses ejected into the duodenum are of the consistency of thick soup. The pylorus acts as a dynamic filter rejecting solid masses of food which pass back into the antrum for further attempts at homogenization (Code, 1962). Some solid materials obviously do pass through, as we can see with radiopaque tablets or biopsy capsules, or by the less elegant proof of observing fruit stones or tomato skins in the stools.

Gastric Juices—Gastric secretion from the body of the stomach is highly acid, containing HCl, proteolytic and some lipolytic enzymes, and intrinsic factor. Antral secretion, on the other hand, is predominantly an alkaline mucous juice.

There is a corresponding histological difference between the two parts of the stomach. The body is lined by a layer of mucous-secreting epithelial cells studded with gastric pits, into which drain several gastric glands (see *Figure 30*). These gastric glands are lined by chief cells which predominate in the neck of the gland, and oxyntic or parietal cells which are most numerous in the main part of the gland. Pepsinogen granules can be demonstrated in the chief cells.

Pepsinogen is the inactive pro-enzyme of pepsin; it has a molecular weight of 42,000 and, at a pH below 5·0, it changes automatically to the active state. The pepsinogen granules decrease after the cells have been stimulated to secrete and gradually reappear when the cells are resting. There is more than one level of optimum proteolytic activity in the stomach, the main one being between pH 1·7 and 2·0, and another between 3·5 and 4·5 or even higher (Schlamowitz and Peterson, 1959). The enzyme that is active in the more acid medium is pepsin, while in the less acid medium, gastricsin—sometimes regarded as a separate enzyme—becomes active (Davenport, 1961). The parietal cells are presumed to be the source of acid secretion, although pure parietal cell secretion has so far eluded collection (Bradford and Davies, 1950; Teorell and Wersäll, 1945). The total acid output of the stomach has been shown to be proportional to the population of parietal cells (Bruce and colleagues, 1959; Card and Marks, 1960).

The mucous membrane of the antrum is also studded with pits but, unlike the gastric glands of the body, they contain no parietal cells; they contain only mucous-secreting and neck-chief cells. A more detailed description of the histology of the normal and abnormal gastric mucous membrane is given in Chapter 6.

The function of the external secretions of the antrum is to protect the cells from peptic digestion.

CONTROL OF SECRETION

The mechanisms of gastric acid and enzyme secretion have been the subject of more study than any other other alimentary function, yet a complete understanding of the physiological processes involved has not been achieved so far. It is the purpose of this chapter to summarize the mechanisms of digestion and absorption in the upper alimentary tract in order to see how these may be affected by operations designed for the cure of ulceration. It is not intended to consider the physio-pathology of peptic ulceration—for this the reader is referred to the works of Ivy, Grossman and Bachrach (1950), and to the exhaustive and explicit chapters by Sircus (in Wells and Kyle, 1960), and by Chapman and Nyhus (in Harkins and Nyhus, 1962).

The following is a brief summary of the mechanisms of control of gastric secretion.

Stimulation

There are two important stimuli, the nervous (as described by Pavlov, 1927) and hormonal (postulated by Edkins, 1906). Vagal stimulation by sham feeding (Pavlov, 1927), or by electrical stimulation in experimental animals (Harper, Kidd and Scatcherd, 1959) or by the production of hypoglycaemia in man (Hollander, 1946 and 1948; Janowitz and Crohn, 1951) produces a copious gastric secretion rich in acid and poor in enzymes. Distension of the antrum either by food or by a balloon stimulates the production of the hormone gastrin which, in turn, acts upon the gastric glands of the body of the stomach effecting the secretion of gastric juice rich in enzymes (Grossman, Robertson and Ivy, 1948).

It is now appreciated that in the normal intact individual the hormonal and nervous mechanisms do not act separately but are reciprocal and intimately inter-related processes. Vagal stimuli act directly on the parietal cells to produce an acid secretion (Linde, 1950) and also on the antrum to stimulate the production of gastrin (Uvnas, 1942; Nyhus and colleagues, 1960). Gastrin is produced even by the vagally denervated antrum in response to distension (Grossman, Robertson and Ivy, 1948), and has two main physiological actions: to stimulate acid secretion by the parietal cell and to sensitize the gastric glands to other stimuli (Chapman and Nyhus, 1962). The injection of histamine into dogs with a Pavlov pouch (innervated) stimulates the secretion by the pouch of both acid and pepsin; whereas the same dose in dogs with a Heidenheim pouch (vagally denervated) stimulates the secretion of acid only (Gregory, 1962). The action of the vagus, therefore, potentiates that of gastrin, and the action of gastrin potentiates that of the vagus.

Regulation

It is quite as important to understand the mechanisms which depress gastric secretion as it is those which stimulate.

Antral Inhibition—The observations which support the hypothesis that acid in the antrum depresses gastric secretion are:

(1) If the antrum remains out of contact with the acid stream, gastric hypersecretion and recurrent ulceration is invariable (Devine, 1928; Ivy, Grossman and Bachrach, 1950).
(2) If such an antrum is perfused with acid, either in dogs or in man, gastric hypersecretion is prevented (Kay, 1958).
(3) Gastric secretion in humans as observed before and after the second stage of a two-stage Billroth II type gastrectomy is found to be reduced by the removal of the excluded antrum at the second operation (Waddell, 1956).
(4) Removal of the antral mucous membrane at the time of the first operation prevents the gastric hypersecretion which otherwise follows the antral exclusion operation (Bancroft, 1932).

It would therefore seem likely that gastric secretion is normally inhibited by the presence of acid in the antrum. The presence of an antral inhibitory hormone has been postulated (Harrison, Lakey and Hyde, 1956; Jordan and Sand, 1957), but many workers have failed to demonstrate the presence of such a substance (Longhi and colleagues, 1957; Woodward and colleagues, 1958; and Dragstedt and colleagues, 1959). Recent cross circulation experiments reported by Thompson and Lerner (1961) have brought fresh evidence to support the belief in the existence of the antral inhibitory hormone.

The protective effect of this 'feed-back' mechanism is obvious, but it is difficult to see why the low antral pH which develops during the digestion of a meal (James and Pickering, 1949), does not prevent further gastric secretion. Presumably the mucous coating effectively protects the chemo-receptors.

Duodenal Inhibition—Sircus (1958) describes two mechanisms by which the duodenum has an inhibitory influence on gastric secretion. The one mechanism is receptive to changes in pH and is mediated through the vagus. The other, receptive to changes in osmolarity, is hormonal.

The vagally mediated acid inhibitory mechanism is thought by Pincus, Thomas and Rehfuss (1942) to be a relatively unimportant factor in the control of acid secretion whilst others, including Hunt (1957), found evidence that this mechanism was defective in patients with duodenal ulcer.

The first hormonal gastric inhibitory agent to be recognized was enterogastrone, produced by the mucosa of the small bowel, particularly the duodenum (Feng, Hou and Lim, 1929). The stimulus required to produce enterogastrone secretion is thought to be either bile salts (Menguy, 1960) or emulsified fat (Sircus, 1958). The passage of fat into the duodenum in normal man results in reduction of acid secretion and reduction of gastric motility and emptying (the enterogastric reflex).

Gastric Digestion

When the food has been adequately chewed and mixed with the ptyalin of the saliva, the amylase digestion continues in the centre of the food mass in the stomach where the pH remains high. Thirty minutes after a meal approx. 50 per cent of the carbohydrate remaining in the stomach is digested, compared with less than 10 per cent of the protein (Beazell, 1941). The boluses of chyme ejected into the duodenum may occasionally contain a proportion of digested protein higher than 10 per cent, but it appears that the main action of pepsin and gastricsin is to break down the walls of the animal cells to allow the proteins, fats and carbohydrates to be dispersed in a form in which they can be digested in the small bowel. Pepsin also hydrolyses dietary proteins to proteases and peptones.

Gastric lipolytic activity is very limited; also, the physical state of the dietary fat in the stomach is unsuitable for digestion. In the acid gastric content, fat is in the form of large globules; it is not until these are emulsified in the duodenum in the presence of alkalis and bile salts that effective digestion occurs.

Gastric Emptying

The waves which pass across the antrum, churning and mixing its contents, usually die out at the pyloric region. The pylorus is not

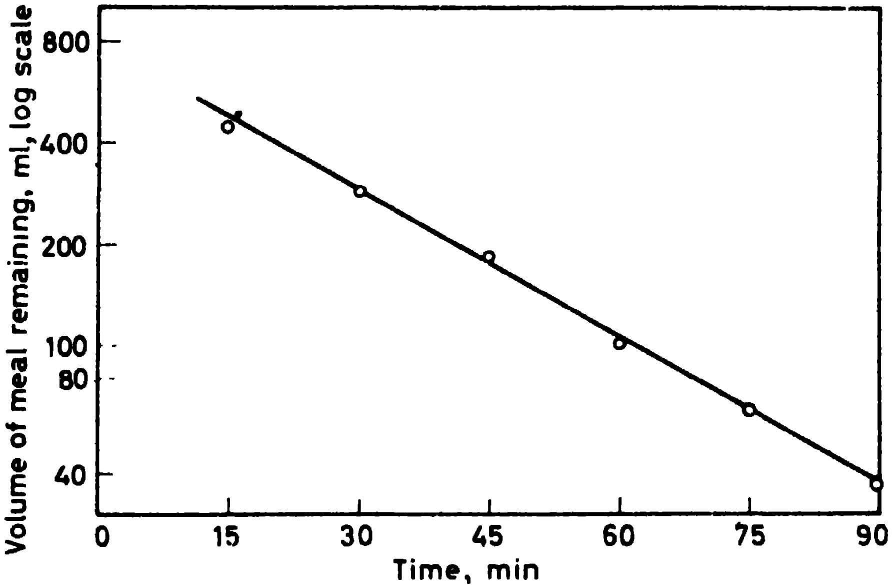

Figure 29. Rate of gastric emptying. Average volume of a 750 ml liquid meal remaining in the stomach, plotted on a logarithmic scale, against time, plotted on a linear scale. (Drawn from the data of Hunt and Spurrell, 1951)

an active sphincteric mechanism which contracts to prevent the onward passage of antral contents, but may rather be considered as the graveyard of gastric peristalsis. The pylorus is the end of the muscular antrum and acts as a functional sphincter by failing to relax before the antral contraction waves. Gastric emptying is effected by the periodic large peristaltic wave which completely subdivides the antrum, sweeping distally and preceded by a wave of relaxation which extends beyond the pylorus into the duodenum.

The rate of emptying the stomach is primarily related to the volume it contains. At the beginning of a meal the rate of emptying is fast and at the end is slow. *Figure 29* shows the figures derived from the work of Hunt and Spurrell (1951), who demonstrated that if the logarithm of the volume remaining in the stomach after a meal is plotted against time, the result is a straight line.

The primary relationship between emptying and volume of gastric content is influenced, however, by a number of intrinsic factors, including temperature, tonicity and composition of the food. Cold foods tend to leave the stomach rapidly whereas gastric emptying is retarded by hot foods. Hypertonic foods are emptied more slowly than hypotonic. Both these mechanisms appear to be designed to protect the duodenal and jejunal mucosae and, although they achieve this to some extent, the efflux through the pylorus is not always isotonic or isothermal. Hypertonic or hot solutions entering the duodenum will stop the movement of most of the villi and elicit secretion of a layer of mucus over the surface (Davenport, 1961). Fat in the stomach is one of the most potent means of retarding gastric emptying; this mechanism appears to function in order to prevent the small bowel being flooded with more fat than it can digest, rather than to protect the mucosa from any noxious influences.

Gastric Absorption

There is negligible absorption of most foodstuffs from the stomach into the blood stream. Water soluble substances—such as glucose and saline—will diffuse across the mucosa from high concentration in the stomach, but the permeability of the barrier is poor. Some fat soluble compounds, however, are more readily diffusible including ethyl and methyl alcohol.

DUODENUM

Ingested food broken up and mixed with gastric juice to the consistency of a thick soup is ejected periodically from the stomach into the duodenum. The important functions of the duodenum are:

(1) The neutralization of the gastric acid.
(2) The emulsification of the dietary fat so that it is susceptible to the action of lipolytic ferments.
(3) The mixing of the chyme and the digestive juices secreted from the pancreas, liver and the duodenum itself. All three functions are carried out simultaneously.

Autonomic innervation is essential for the proper functioning of the duodenum and its associated glands, but the exact effect of the vagus on these organs is less clearly understood than it is on the stomach. Vagal stimulation in experimental animals leads to increased secretion by the pancreas and duodenal glands, and to contraction of the gall-bladder, these effects being blocked by atropine. All the effects of vagal stimulation can be produced, however, by humoral stimuli but, as in the stomach, the most efficient physiological function is dependent upon the integration of nervous and hormonal mechanisms.

The Secretion of Digestive Juices

Acid in the Duodenum—The presence of acid in the proximal duodenum is the most powerful stimulus for the production of secretin. Secretin (one of the first hormones to be isolated) is a polypetide which can be extracted from all parts of the small bowel, but is found predominantly in the duodenum. Its action is to stimulate a copious flow of alkaline pancreatic juice. Even in its purest form it will also stimulate the production of bile by the liver. Secretin-stimulated .pancreatic juice, although containing some enyzmes, is principally alkaline pancreatic secretion. It is probably the major factor in neutralizing gastric acid and rendering duodenal contents alkaline. While vagal innervation is not essential for the production or action of secretin, experimentally the mechanism is less efficient after vagotomy.

Food in the Duodenum—Some of the initial out-pouring of pancreatic juice which accompanies the taking of food is stimulated by nervous mechanisms via the vagus. Sham feeding in dogs results in an early but short-lived pancreatic secretion of juice rich in amylytic, proteolytic and lipolytic ferments. The chief effect of this juice is to act upon the first chyme to pass through the pylorus and to break down the proteins to peptones and amino acids. These latter are in their turn potent stimuli to the further production of enzyme juice by the pancreas, and so duodenal digestion is prepetuated. This peptone stimulation is mediated by pancreozymin, an enzyme which has not yet been isolated in a pure form.

The presence of fat in any form in the duodenum is a powerful stimulus to gall-bladder contraction, a reflex controlled by the hormone cholecystokinin (again of unknown composition). The presence of bile salts in the duodenum, which then results, is a powerful stimulus to further bile secretion by the liver.

Duodenal Digestive Juices

The pancreas is probably the most important producer of digestive ferments. Small-intestinal juice, or *succus entericus*, is something of an enigma. There is a copious flow of fluid to and fro across the intestinal mucosa, but the actual secretion of digestive juices has not yet been proved. Much of the work done in estimating the enzymes found in the small bowel has failed to eliminate or has overlooked the intra-cellular enzymes liberated by exfoliation or by the trauma of collection. The only true glands of the small intestine are the Brunner's glands which are found in the sub-mucosa with decreasing frequency from the juxta-pyloric duodenum to the mid-jejunum. These glands secrete a viscid alkaline juice containing, among many other enzymes, enterokinase. The small volume of this secretion means that it has a negligible neutralizing effect. Its role is probably more important as a surface protection than as a source of digestive ferments.

Duodenal Digestion

The Function of Pancreatic Enzymes—Total removal of the pancreas is usually incompatible with normal digestion of proteins and fats unless active pancreatic enzymes are given by mouth. Occasionally, however, cases have been reported when fat absorption was as high as 71–92 per cent after total pancreatectomy (Davenport, 1961); so pancreatic enzymes are not always indispensable.

Pancreatic enzymes are of three main groups: amylytic, lipolytic and proteolytic. There are also many minor enzymes. Amylytic activity is associated with at least two enzymes, the most important of which is alpha-amylase which is similar in action to salivary alpha-amylase. Proteolytic activity in fresh uncontaminated pancreatic juice is negligible since the enzyme precursors require activation. When activated, there are at least four enzymes, including trypsin and chymotrypsin. The pancreas also secretes an inactivator which is effective in inhibiting the action of the proteolytic enzymes, particularly trypsin.

The proteolytic enzymes share many functions in protein digestion, but each has a characteristic action in hydrolysing certain bonds in the different protein molecules and so each has its part to play in the complete and efficient breakdown of dietary protein to amino acids and polypeptides.

Pancreatic lipase breaks down the dietary fats which are mainly in the form of triglycerides. Other enzymes such as lecithinase-A act on the phospholipid bonds. Lipase can act most efficiently when the fat is dispersed into fine globules, for this increases the surface area available for enzyme action. Fat is normally delivered into the duodenum in amounts not exceeding 8–12 g/h, regulated by the 'feed-back' mechanisms previously mentioned. Since the gastric acid effectively destroys most ingested emulsions, fat in the stomach is in the form of large globules. The first step in duodenal fat digestion is therefore emulsification. Once gastric acid is neutralized this is achieved by the emulsifying agents, the most important of which are bile salts. The early products of digestion, monoglycerides and fatty acids, further stabilize the emulsion. Normally, fat digestion is very efficient, and over half the dietary fat is digested before the meal leaves the duodenum (Borgström and colleagues, 1957).

Small Intestine—The function of the small intestine is primarily absorptive. Each day, for example, approximately 9 l. of fluid enters the small bowel from the stomach, from glandular secretions or across its own wall, and less than 1 l. normally passes on into the colon. Comparatively little absorption takes place in the colon, even of water. The structure of the small bowel is ideally suited for absorption, a very large surface area being achieved by mucosal folding and the projecting villi. Indeed, it has been estimated that the area of the small intestinal mucosa is 75,000 cm^2 (Grim, quoted by Davenport, 1961). Nature's generous provision is evident when it is found that it is possible for man to maintain normal nutrition after removal of one-half of the small bowel.

Digestion and absorption of carbohydrates, proteins and fats is normally so efficient that over 50 per cent has been absorbed by the time the meal has entered the upper jejunum and 90 per cent by the mid-jejunum (Borgström and colleagues, 1957).

Intestinal Motility—The pylorus has been called the graveyard of peristalsis (Code, 1962).

Movement caudally in the small bowel is normally not by peristalsis, but by segmentation (Cannon, 1911). The peristaltic waves shown by Bayliss and Starling (1899) in the cat intestine are artificial in that they are stimulated by solid boluses, not by the normal liquid content of the small bowel. Similar artificial peristaltic reflexes can be stimulated in man by distending a balloon within the lumen. Code has recently re-stated Cannon's concept of movement by segmentation, and suggests that the differential rate of segmental contraction—11 per min in the duodenum to 6 per min in the ileum (Code, 1962)—is the factor which ensures the steady onward progression of the meal, the segmentation, at the same time, ensuring the adequate mixing of food and digestive juices.

Intestinal Absorption—Huge volumes of water and accompanying electrolytes, sodium, potassium, chloride and bicarbonate, pass to and fro across the intestinal mucosa so that the net gain of these substances by the body is the result of the small excess of the gross gain over the gross loss. For instance, if isotonic sodium chloride solution, containing radio-active sodium, is placed in an experimentally prepared intestinal loop the total sodium content of the loop remains relatively constant, but the radio-active sodium is rapidly distributed through the body (Visscher, 1944, quoted by Davenport, 1961). The net absorption of water, sodium, potassium and chloride is maximal in the upper small bowel and becomes progressively less, distally.

Certain inorganic ions and foodstuffs are absorbed by active transport mechanisms of varying complexity. The absorption of fats, proteins, iron, calcium and vitamin B_{12} will be considered in the chapters dealing with specific metabolic defects after gastrectomy and will, therefore, only be considered briefly here.

Carbohydrate—High concentration of glucose and galactose in the stomach will result in some diffusion into the blood stream and some dilution of the hypertonic solution in the stomach. The mucosa of the small intestine is much more permeable, however, and the passage of fluid into the gut to restore isotonicity and the passage of glucose into the blood both occur rapidly. Normally, food is taken in the form of a mixed meal containing fats, proteins and carbohydrate and the passage of the meal into the duodenum is regulated by its fat content. If hypertonic glucose drinks are taken, however, the first bolus to pass into the duodenum will cause a reflex inhibition of gastric emptying (see above) so that in the normal state there is a regulating mechanism determining the rate of absorbable sugars discharged into the duodenum.

It has already been seen that salivary digestion of carbohydrates in a mixed meal continues in the stomach and that up to 50 per cent of the carbohydrate is digested. The pancreatic amylases rapidly hydrolyze the remaining carbohydrate to the resultant simple sugars, mostly glucose. The hydrolysis of sugars increases their osmotic pressure and this results in the retention of fluid within the lumen of bowel until the absorption of the sugars has taken place.

Glucose and galactose are absorbed by an active transport mechanism which requires the expenditure of energy and the consumption of oxygen, but allows the absorption against a concentration gradient. Other sugars such as xylose, fructose and ribose are absorbed by diffusion (Wilson and Vincent, 1935; Wilson and Landau, 1960). The absorption of glucose from the small bowel does not involve phosphorylation, nor is it dependent upon its concentration, the presence of insulin or the blood sugar level

(Davenport, 1961). The digestion and absorption of fats and proteins are discussed in Chapter 10, that of iron, folic acid and vitamin B_{12} in Chapter 8 and that of calcium in Chapter 9.

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THE EFFECTS OF GASTRIC OPERATIONS ON THE GASTRIC MUCOSA

C. Tasman Jones and John A. Williams

Before the introduction of instruments for obtaining satisfactory per-oral biopsy specimens, the only opportunity for examining the histology of the mucosa of the gastric remnant or adjacent small bowel after gastrectomy was afforded by the need for further gastric surgery or by post-mortem examination. Because of the early onset of autolysis of the intestinal mucosa, post-mortem examination is usually unsatisfactory. Tube biopsies, pioneered by Jackson (1907), were subsequently developed by him and his son (Jackson and Jackson, 1935) who applied their early tube biopsy technique almost exclusively to the diagnosis of gastric carcinoma.

Tube biopsies for non-carcinomatous lesions were not widely used until the introduction by Wood and colleagues (1949*a*) of a suction biopsy tube incorporating a knife blade (see *Figure 38*). Thus began a new era in which our knowledge of gastro-intestinal histology is still expanding. Since that time a number of instruments have been produced which make it possible to obtain, with safety, small pieces of bowel mucosa for immediate fixation. Our own observations have been made using the 'Crosby capsule' and 'Wood's tube', and brief mention of the technique employed is made on p. 136.

A short account of the histology in the normal and pre-operative ulcer patient will be followed by some observations made after partial gastrectomy. For detailed descriptions of gastric mucosal histology and pathology the reader is referred to the work of Palmer (1954) and Wood and Taft (1958).

The possibilities of investigating and co-relating gastric pathology and function after partial gastrectomy is interesting an increasing number of workers so that any conclusions drawn from a limited series of observations may soon be invalidated or at least altered in the light of new knowledge.

NORMAL GASTRIC HISTOLOGY

Detailed accounts of gastric histology have been given by Bensley (1928), Plenck (1932) and Maximow and Bloom (1948).

The mucous membrane of the stomach is lined by a layer of tall columnar mucous-secreting epithelial cells. There is an abrupt change from oesophageal mucosa at the cardia and to duodenal mucosa at the pylorus. The entire mucosal surface of the stomach is studded with minute pits, into which open the gastric glands. The structure of these glands differs in the three areas of the stomach.

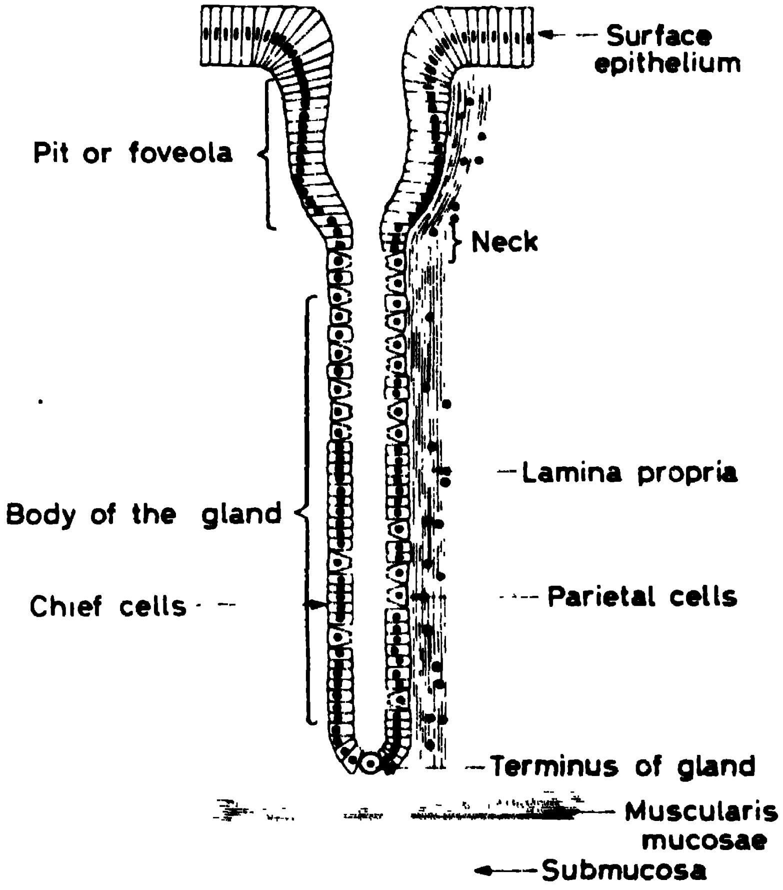

Figure 30. Schematic representation of principal gastric gland (after Palmer, 1954)

Cardiac Area of the Fundus

Cardiac glands are found within 1–4 cm of the cardio-oesophageal junction. These are shallow and lined by mucous-secreting cells only.

Body and Fundus

Chief glands (or principal gastric glands) are found throughout the body and fundus from the cardiac glands above to the pyloric glands below. They are long, tortuous and sometimes branched, several opening into each gastric pit. They contain oxyntic (parietal) cells and zymogenic (chief) cells and relatively few apparently unspecialized mucous cells (*Figure 30*).

The parietal cell, found predominantly near the neck of the gland, is pyramidal in shape with its apex towards the lumen of the gland. It is larger than the other glandular cells and it is characterized by the presence of oxyntic granules. Under the electron microscope these granules can be recognized as mitochondria which are arranged around intra-cellular canaliculi (Wyburn and Hally, 1961). These canaliculi transport the secretions of the oxyntic granules to the lumen of the gland.

There is strong presumptive evidence that the parietal cells are responsible for the secretion of hydrochloric acid although, so far, it has not been possible to collect pure parietal cell secretion.

The zymogenic cells are characterized by the appearance of a basophil substance in the base of the cell and of secreting granules in the apical cytoplasm. The granules termed 'pepsinogen granules', consist of nucleoprotein and are concerned with the synthesis of pepsin.

After prolonged gastric secretion the 'pepsinogen granules' almost disappear but rapidly return when the secretion stimulus is removed.

Antrum

The antrum is lined by pyloric glands which, like the chief glands, are branched. The glandular layer, however, is not as thick as in the body and the glands do not contain parietal or chief cells. The extent of the pyloric glandular area is extremely variable. In a normal person it extends from 2 to 16 cm up the lesser curve from the pylorus and about 4 cm less up the greater curve (Oi, Oshida and Sugimura (1959). The change from pyloric gland to chief gland area may be fairly abrupt but, more commonly, there is an intermediate zone with—as the term implies—a gradual transition from one gland type to the other. The pyloric gland area does not necessarily correspond with the anatomical antrum. It is assumed that gastrin is produced in the mucosa of the pyloric glands, but it is not yet known whether the cells responsible for gastrin production extend over the whole of the pyloric gland area; it appears likely that gastrin is produced in a smaller juxta-pyloric area (Capper and colleagues, 1962).

CHANGES IN THE SIZE OF THE PYLORIC GLAND AREA IN PATIENTS WITH PEPTIC ULCERATION

In patients with duodenal ulcer the pyloric gland area appears to be small and the chief gland area large. In those with severe duodenal ulcer stenosis or with gastric ulcer, the area of pyloric type glands is greater than normal and may extend right up the lesser curve to be confluent with the cardiac gland area. It is possible that such a diminution of the chief gland area is due to metaplasia as a result of inflammation, for pyloric (duodenal ulcer) stenosis may also be associated with gross inflammatory changes.

GASTRITIS

In studies of the aetiology of chronic gastritis Palmer (1954) and Joske, Finckh and Wood (1955) recognize six different histological groups: slight superficial gastritis; moderate or severe superficial gastritis; superficial gastritis with atrophy; atrophic gastritis; severe atrophic gastritis; and gastric atrophy. Other descriptive terms have been used to describe the appearances of the gastric mucosa, including the terms hypertrophic and lymphocytic gastritis. Because of the difficulties of exact identification of the limits of each of these groups we prefer to grade our gastric biopsies according to the severity of the inflammatory signs on the one hand, and of loss of gastric specificity, i.e. atrophy, on the other. In order to compare the effect on the gastric mucosa of different operations there seems good reason to simplify the grading of the pathological changes.

INFLAMMATION

Chronic gastritis may be classified into three overlapping groups: mild, moderate and severe [see Plate I(*a*) and (*b*)].

Mild Gastritis

There is no significant alteration of glandular pattern (*Figure 31*). Small numbers of lymphocytes and plasma cells infiltrate the interstitial spaces, particularly around the necks of the glands, while the muscularis mucosae is relatively unaffected.

Moderate Gastritis

The mucosal pattern is moderately distorted with thickening and more marked round cell infiltration (*Figure 32*). The inflammatory process extends through and may disrupt the muscularis mucosae. Some of the infiltrating cells may be polymorphonuclear leucocytes.

Severe Gastritis

Marked distortion of the mucosal pattern results from an asymmetrical distribution and shortening of the glands (*Figure 33*). The

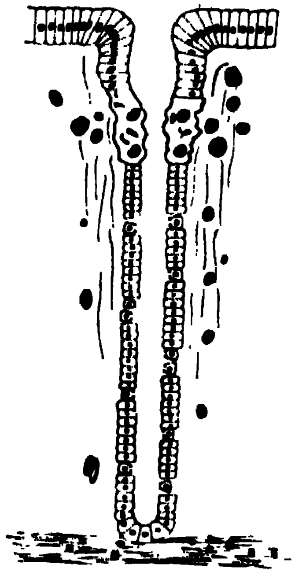

Figure 31. Mild gastritis
(after Palmer, 1954)

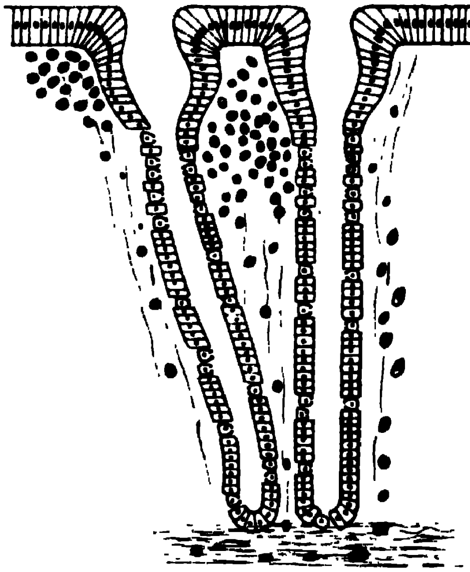

Figure 32. Moderate gastritis
(after Palmer, 1954)

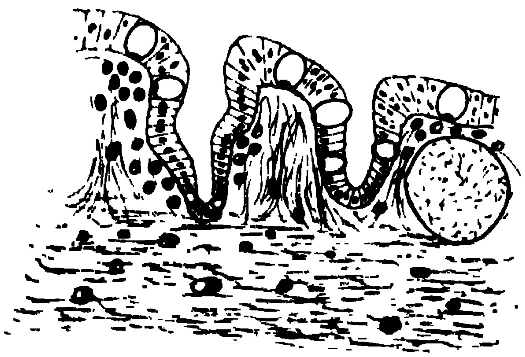

Figure 33. Severe gastritis
(after Palmer, 1954)

stroma is heavily infiltrated with inflammatory cells and there are many lymphoid follicles, some with active germinal centres. Fragmentation of the muscularis mucosa is seen secondary to inflammation and fibrosis (Deutsch and Christian, 1959).

ATROPHY (*Figure 34*)

Loss of Specific Gastric Gland Characteristics

In particular, the disappearance of oxyntic (parietal) and zymogenic (chief cells) is often referred to by the misleading term 'gastric atrophy', when what is meant is atrophy of the specialized secretory cells. This degenerative change is seen typically in the stomach of patients with pernicious anaemia. Associated with, but apparently independent of, the loss of specific cells, another change which may be observed is the increase in the number of mucous secreting goblet cells, so that the principal gastric glands come to be indistinguishable from the pyloric glands, or even to resemble the mucosal pattern of the colon. This latter resemblance has led to the use of the term 'intestinalization' or 'intestinal metaplasia'. The development of gastritis, particularly severe gastritis, is often associated with signs of loss of specificity or intestinalization. This suggests a causal relationship: 'atrophy' following inflammation (Palmer, 1954; Wood and Taft, 1958). However, some biopsies show complete loss of specific secretory cells with little or no evidence of inflammation or its fibrotic sequelae. It is possible to postulate two types of 'atrophy' —one post inflammatory and the other idiopathic (e.g. pernicious anaemia).

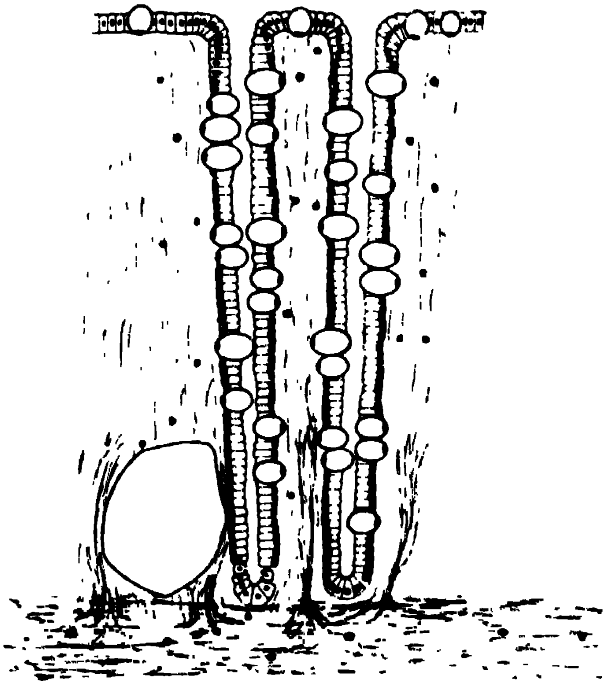

Figure 34. Gastric 'atrophy' (after Palmer, 1954)

The Effects of Age

Evidence that this loss of specialized secretory cells and intestinal metaplasia is degenerative is provided by the fact that such changes are not observed in infancy, are rare in childhood and are seen with increasing frequency with advancing age (*Figure 35*). While the stomachs of some elderly patients show very little inflammatory change, there is generally at least a diffuse round cell infiltration.

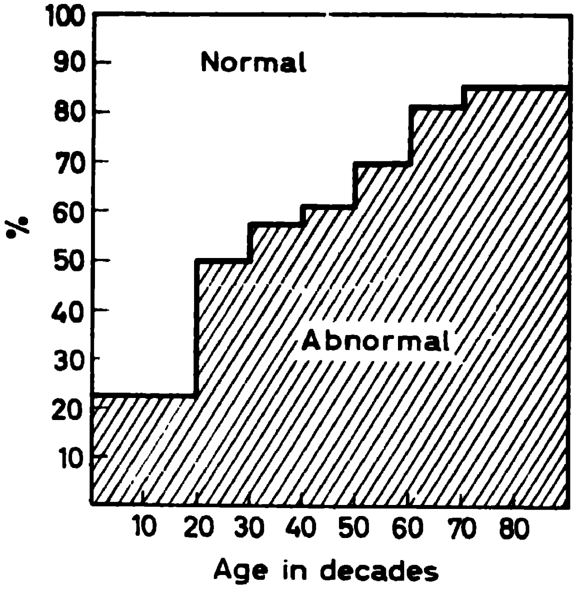

Figure 35. Gastric biopsy appearances (after Joske, Finckh and Wood, 1955)

Palmer (1954) emphasized that although the incidence of gastritis is more common with increasing age, gastritis is not a sign of age but of disease.

Mucosal Changes in Chronic Gastric and Duodenal Ulceration

Gastric biopsy affords a more accurate assessment of the state of the mucosa than does gastroscopy. By gastroscopic examination Palmer (1954) showed that of a group of patients with active duodenal ulceration, but without pyloric obstruction, 16 per cent had some areas of chronic superficial gastritis, while biopsy specimens from the same group of patients revealed abnormal histology in just under 50 per cent.

According to Joske, Finckh and Wood (1955) patients with gastric ulcers have marked histological changes; about 33 per cent have superficial gastritis and 66 per cent have severe or atrophic gastritis. With duodenal ulceration 60 per cent have a normal biopsy, 33 per cent superficial gastritis and only a small number have atrophic gastritis (Doig and Wood, 1952).

The Effect of Gastric Operations on the Gastric Mucosa

In 1932, Hurst commented on the association between gastroenterostomy and the onset of achlorhydria. He thought that mucosal atrophy occurred as a result of the gastro-jejunal anastomosis and that this atrophic change was reversible.

Auguste and Paris (1947) found that immediately after Billroth II partial gastrectomy the incidence of achlorhydria was dependent, very largely, on the condition for which the operation was performed; for gastric ulcer 72·7 per cent and for duodenal ulcer, 36·8 per cent. In cases examined some years after operation the incidence of achlorhydria was more nearly equal; for gastric ulcer 93·7 per cent and for duodenal ulcer 74 per cent.

Palmer (1948), studying by gastroscopy the effects of gastric operation on the gastric mucosa, reported that there was an immediate post-operative gastritis which settled after a few weeks or months but that even after the gastroscopic appearance had returned to normal, the biopsy findings were usually those of inflammation. He found that gastrostomy or gastrotomy in themselves did not produce gastritis, but that gastro-enterostomy did. Impressed by the incidence of gastritis before operation in patients with ulcers, he suggested that the inflammatory changes were, in part, a natural progression after operation of processes at work before. However, in a later study (Palmer, 1953) he produced very strong evidence that the mucosal changes were due to the operation when he reported 84 patients with duodenal ulcers studied for periods of up to four years after an operation at which their gastric mucosa was found to be normal. Of the post-operative biopsies 54·6 per cent were abnormal. After Polya (Billroth II) operation 60·7 per cent became abnormal, after vagotomy and gastro-enterostomy 46 per cent, and after gastro-enterostomy alone 90 per cent (of only ten cases) were abnormal. Palmer stated 'the only common denominator permitting co-relation with this common disease process (of gastritis) was the presence of the surgical gastro-enteric fistula'.

Soon after the publication of Palmer's work there were many reports in the literature of gastritis following partial gastrectomy. Debray, Naumonier and Housset (1956) claim that the incidence of mucosal changes is four to six times as great after gastrectomy as in patients with other gastro-intestinal diseases.

Lees and Grandjean (1958), reporting their findings on gastric biopsy in 33 non-anaemic post-gastrectomy patients, found only one normal biopsy. They reported no significant difference with time after operation but all their patients operated on for gastric ulcer had severe changes. Coghill and Williams (1958) and Deller, Richards and Witts (1962) reported similar high incidences of gastritis after partial gastrectomy.

As a cause of post-operative gastritis, the weight of evidence seems to be overwhelming in incriminating gastric resection operations in general and gastro-jejunal anastomoses in particular.

Relationship of Gastric Histology to Function

There is a close co-relation between the histological findings of gastric biopsy and both resting gastric acidity and maximal histamine response (Wood and colleagues, 1949b). There is also a close relationship between the production of gastric acid and the production of intrinsic factor. Intrinsic factor production is decreased after partial gastrectomy, as judged by the patient's ability to absorb radio-active vitamin B_{12} and the response of that absorption to the oral administration of hog intrinsic factor (Lous and Schwartz, 1959; Deller and Witts, 1962; and Jones and colleagues, 1962).

The possible causes of this gradual 'atrophy' of the gastric glands are:

(1) Gastritis as the result of the reflux of duodenal secretions.
(2) Gastritis as the result of infection (stasis, the loss of gastric acid and an infected afferent loop may be pre-disposing factors).
(3) Chronic iron deficiency (see Chapter 8).
(4) Loss of secretory stimuli due to: (*a*) vagotomy; (*b*) removal of the gastrin secreting antrum. Other less likely possibilities are:
(5) A genetic pre-disposition to atrophy in patients with peptic ulceration. This view put forward by Palmer (1948) was later invalidated by his own work (Palmer, 1953). Also, patients with pernicious anaemia do not usually give a history of peptic ulceration (Cox, 1962; see Chapter 8).
(6) Vitamin B_{12} deficiency in itself may possibly pre-dispose to gastric atrophy. After adequate B_{12} therapy, however, there is no improvement in gastric glandular atrophy seen on biopsy (Finckh and Wood, 1953).

THE AUTHORS' SERIES

In a current investigation, 56 patients have so far been studied, all more than five years after different operations for gastric or duodenal ulceration. Per-oral gastric biopsies have been obtained with a modified 'Crosby capsule' or, as has been our recent practice, with a 'Wood's tube'. The histological sections of these biopsies have been examined and graded independently by both authors without knowledge of the source of the specimen. In order to compare the effects of different types of operation, broad groups were chosen. The inflammatory changes were classified as: (1) mild or moderate; and (2) severe. The signs of atrophy of specific secretory cellular function were similarly graded as: (1) mild or moderate; and (2) severe. In six cases more than one gastric biopsy was obtained and, in all six, the appearances were the same in the two samples. Joske, Finckh and Wood (1955) report that in 726 instances where two or more biopsies were taken 73·8 per cent were essentially similar.

Results

Nineteen operations were for gastric ulcer, 32 for duodenal ulcer, 3 for both and 2 for stomal ulcer. In order to achieve as large groups as possible for this interim analysis, we are only considering the findings in three types of operation:

(1) Billroth I operation for gastric ulcer (16 cases).
(2) Billroth II operation for duodenal ulcer (18 cases).
(3) Vagotomy for duodenal ulcer (8 cases, 2 of which also had a gastro-enterostomy)

The findings in these three groups are depicted graphically in *Figures 36* and *37.*

Atrophic Changes

The effects of chronic iron deficiency on gastric mucosal structure are discussed in Chapter 8. Atrophic changes are seen most commonly after the Billroth II operation for duodenal ulcer (*Figure 36*). According to the available data (Palmer, 1954; Joske, Finckh and Wood, 1955) the incidence of atrophic changes is higher in patients with gastric ulcer than in those with duodenal. It is likely, therefore, that in those patients having had a Billroth II operation (gastrojejunostomy) for duodenal ulcer there is a factor which is particularly active in causing the development of specific cellular atrophy. In the small number so far studied, i.e. the gastrectomy groups (1) and (2), there is no significant difference in the mean ages, nor is there any significant difference in the incidence of iron deficiency. In both these groups the antrum has been removed and the remaining stomach remnant still has vagal innervation. Gastric remnant stasis is unlikely to be a factor in either type of operation; the bacterial content of the stomach has not been measured in these two groups. It is most likely, therefore, that the factor responsible for the atrophic changes is the reflux of duodenal and jejunal juices, which is more likely to occur in the Billroth II operation than in the Billroth I. No measurement of the degree of regurgitation into the stomach in the two types of operation has, so far, been attempted.

The low incidence of atrophic changes in the vagotomy group (3) is in striking contrast to that in the other two groups. In patients having had a vagotomy, compared with those having had a gastrectomy, there is a significantly lower incidence of iron deficiency (see Chapter 11) but no significant difference in the age distribution. Those having had vagotomy have not had the gastrin-producing antrum removed, but both the body of the stomach and the antrum are, of course, vagally denervated. The incidence of gastric stasis is probably higher after vagotomy but we have not made a study of the bacterial content of the stomach. It would therefore appear that the three factors protecting the mucosa of the vagotomized patient from atrophic changes are the low incidence of iron deficiency, the absence of duodenal reflux and an intact antrum.

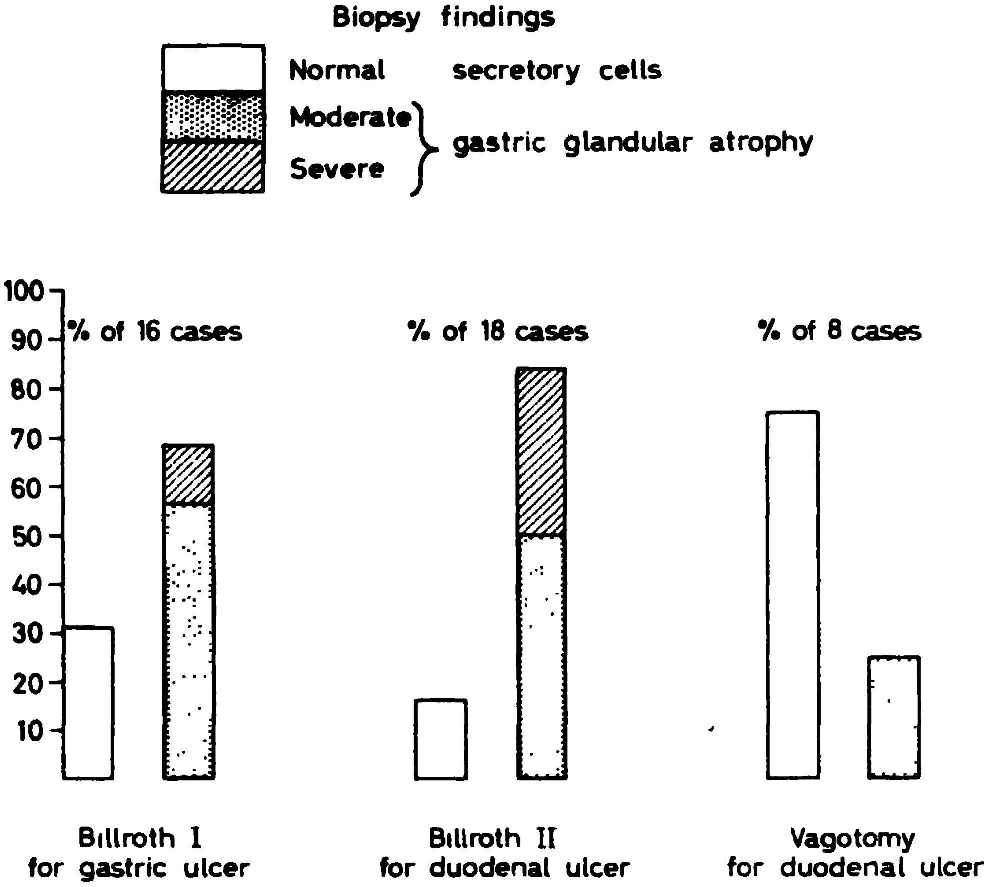

Figure 36. Atrophic changes

Inflammatory Changes

The distribution of the incidence of inflammatory changes in the three groups is different from that of the atrophic changes (*Figure 37*).

The only group in which there was absence of any inflammatory changes was that in which a Billroth I operation had been performed. The high incidence of inflammatory changes in the vagotomy group suggests that gastric stasis may play a part in the genesis of gastric inflammation but that it is not so potent as the reflux of duodenal secretion in the production of gastric glandular atrophy. This hypothesis requires proof.

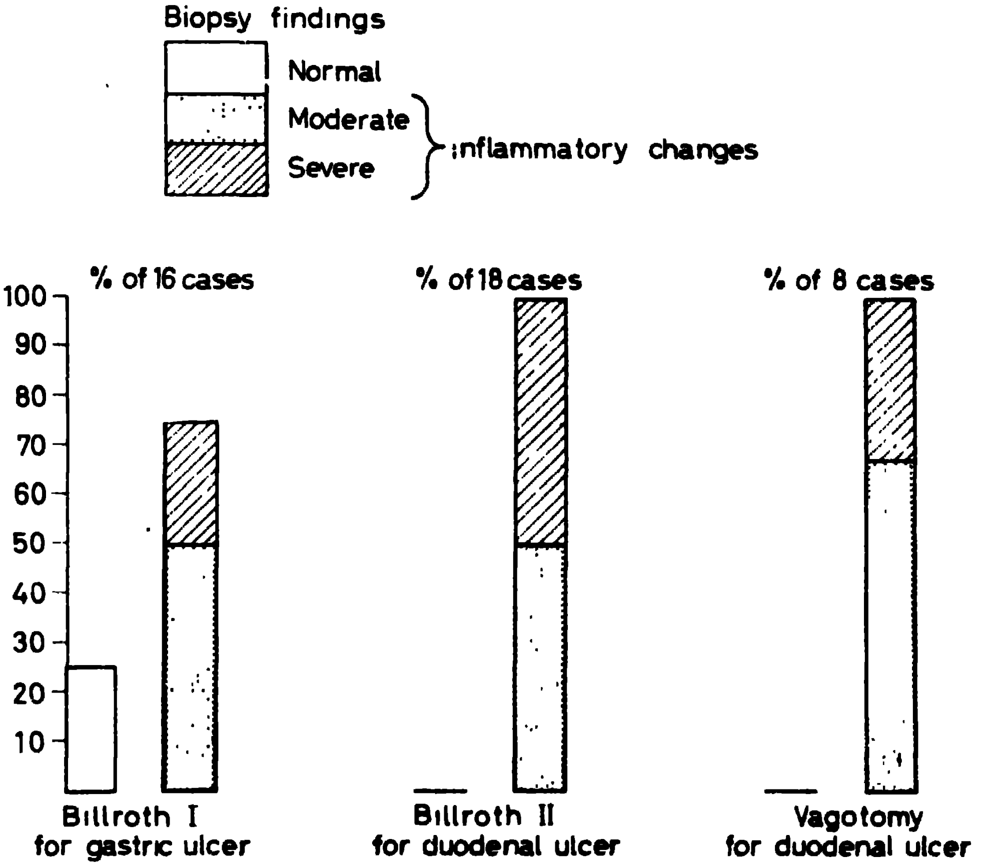

Figure 37. Inflammatory changes

IS PARTIAL GASTRECTOMY CARCINOGENIC?

The idea that chronic gastritis is a pre-cancerous condition was first postulated by Konjetzny (1928). It was later attacked by Guiss and Stewart (1943) but has recently been revived as a result of the work of Morson (1955) in this country. He studied the incidence and distribution of areas of intestinal metaplasia in the stomach of patients with duodenal and gastric ulcers. On the greater curvature of the stomach, metaplasia is seen in only 9·6 per cent of duodenal ulcer cases, in 39·3 per cent of gastric ulcer, and in 66·7 per cent of cases of gastric carcinoma. As a result of a careful histological study he concludes that 30 per cent of gastric carcinomata arise from areas of intestinal metaplasia in the gastric mucosa.

Morson's view is questioned by some Australian workers; Fairley and colleagues (1955) followed 32 patients with chronic gastritis for five years and found no evidence of the development of carcinoma. However, the numbers are too small and the follow-up is too short to give much significance to these findings.

We have seen that gastritis, mucosal atrophy and intestinal metaplasia are likely to develop after gastric operations, particularly where there has been a gastro-jejunal anastomosis. Therefore, if Morson's views are correct it seems logical to argue that after partial gastrectomy a higher incidence of gastric carcinoma might be expected than in the same patients had they had no operation.

DOES DUODENAL ULCER PROTECT?

Natural Decreased Susceptibility

It would be wrong to expect the post-operative incidence of carcinoma to be necessarily higher than in the general population, for there is evidence which suggests that present or previous duodenal ulceration reduces the risk of subsequent gastric carcinoma. Subjects with blood group O have a 40 per cent higher liability to duodenal ulcer than do those belonging to other A B O groups (Aird and colleagues, 1954; Clarke and colleagues, 1955; Buckwalter and colleagues, 1956). On the other hand, pernicious anaemia and carcinoma of the stomach are more common in those with blood group A than in subjects of any other group (Aird, Bentall and Roberts, 1956). It would therefore appear that the majority of gastric operations are performed on patients with a decreased susceptibility to gastric carcinoma. The hypothesis of Eusterman and Balfour (1935) and Bockus (1946), that the presence of duodenal ulceration is some insurance against gastric carcinoma, receives support from the figures of Fischer, Claggett and McDonald (1947), who reviewed the Mayo Clinic records from 1911 to 1945, and Jennings (1963), who reports a prospective study from the London Hospital. Fischer, Claggett and McDonald found records of 13,000 patients with carcinoma of the stomach, 45,000 with duodenal ulcer and only 48 who had a combination of the two diseases.

In a ten-year follow-up of 351 patients with gastric ulcer and 319 with duodenal ulcer, Jennings (1963) found only one patient who died of gastric carconima and this man had had a partial gastrectomy. The expected mortality from carcinoma in 'all males' of the same age distribution is 3·5–4 per cent.

The Incidence of Carcinoma of the Stomach After Gastric Operations

Crohn (1927), reporting a follow-up of 1,025 patients after gastro-enterostomy, found 22 in whom gastric carcinoma had subsequently been diagnosed. Since most operations were for duodenal ulceration, the incidence of carcinoma in this series is probably higher than might be expected. Kühlmayer and Rokitansky (1954), reviewing several thousand autopsies performed in Vienna between 1934 and 1952, found that the incidence of carcinoma of the stomach in patients who had had previous gastric resections was 11 per cent, twice as high as in the normal population. Helsingen and Hillestad (1956) followed 229 post-gastrectomy patients for periods of up to 37 years and found that, in those patients operated upon for gastric ulceration, the incidence of subsequent gastric carcinoma was three times as high as that in the normal population.

More than 100 cases have been reported in the literature of gastric carcinoma developing in patients who have had previous gastric operations for benign ulceration of the stomach or duodenum (Gray and Lofgren, 1949; Debray and colleagues, 1950; Freedman and Berne, 1954; Ryan and Beal, 1957; Aronson and Darling, 1959; Berkowitz, Cooney and Bralow, 1959; de Jode, 1961; and Gibbs, 1962). In most of these reports the development of carcinoma was reported only if it was diagnosed more than five years after the gastric operation, since in those diagnosed soon after the operation it might be argued that the carcinoma was present at the time of operation. The mean interval between operation and the diagnosis of carcinoma is approximately 17 years (Freedman and Berne, 1954). From these isolated reports it is not possible to determine whether the operation had been a pre-disposing factor but the evidence of Kühlmayer and Rokitansky (1954) and Helsingen and Hillestad (1956) suggests some causal relationship. There is an obvious need for further statistical data to elucidate this extremely important problem.

SUMMARY

Disappearance of parietal and chief cells from the gastric glands is associated with loss of the specific secretory function of the stomach (acid–pepsin and intrinsic factor production). These changes, described as gastric glandular atrophy, are influenced by a number of factors, including the age, the diet and race of the patient, the presence or absence of iron deficiency and the presence or absence of inflammation (gastritis). Gastritis also may be caused by one or more of a number of factors including irritating foods, alcohol, tobacco, gastric stasis, infection and small bowel reflux.

Gastric glandular atrophy is most common in those patients with gastric carcinoma, less common in those with simple gastric ulceration, and least common in patients with duodenal ulceration. When patients with peptic ulceration undergo a gastric operation the degeneration of the gastric glands is accelerated. The deterioration is potentiated by the reflux into the gastric remnant of duodenal or jejunal contents and by iron deficiency consequent upon the operation. It is possible—but not yet proven—that the degeneration of the gastric mucosa may pre-dispose to the development of gastric carcinoma.

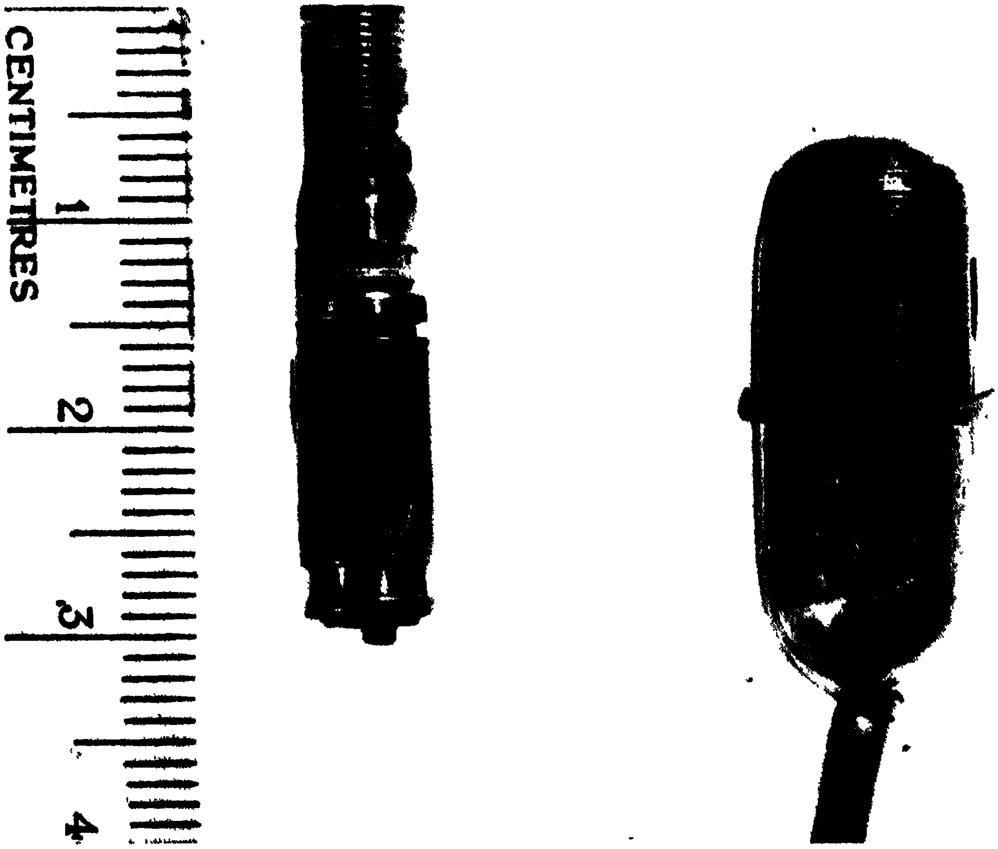

Figure 38. Close-up view of biopsy head: left, Wood's tube; right, Crosby capsule

TECHNIQUE OF TUBE BIOPSY

Most of our examinations are made on fasting non-sedated out-patients. The pharynx is anaesthetized by the patient sucking two amethocaine lozenges (B.P.) for 10 min before the instrument is passed.

The Wood's Tube (Figure 38)

Wood and Taft (1958) advocate the preliminary emptying of the gastric contents before the passage of the biopsy tube. In the post-gastrectomy patient there is usually little resting secretion and we usually omit this preliminary step. With the patient sitting, the instrument is 'measured' against the patient by holding the head of the tube against the tip of the xiphisternum and marking the tube with the fingers at the level of the lobe of the patient's ear. The well lubricated biopsy tube is now passed to this mark; the biopsy head then usually lies within the gastric remnant. A 20 ml syringe is attached to the suction end of the tube and mucosa is sucked into the hole at a pressure of 15 kg/cm^2 and the biopsy cut by pulling, sharply, the wire attached to the cylindrical knife blade. The instrument is rotated and advanced 2–4 cm and a second biopsy cut. After withdrawing the tube and unscrewing the head the biopsy specimens are ejected, suspended in saline and examined under the dissecting microscope. The presence or absence of villi identifies the source of the specimen, and the character of any villi is noted. The biopsy is then immediately fixed in 10 per cent formal saline. If jejunal mucosal specimens are required the tube can be passed a further 10–15 cm and the operation repeated.

The Crosby Capsule (Figure 38)

This biopsy capsule has the advantage that it can be swallowed comfortably by the patient and gives a large biopsy specimen. Practice is required in setting the instrument, and considerable care is needed in its maintenance. The Crosby capsule is eminently suitable for small bowel biopsy in patients with an intact upper gastro-intestinal tract, and we have used it for all our small instestinal biopsies reported in Chapter 7. It is possible to obtain a satisfactory gastric biopsy specimen with this instrument by employing polyethylene tubing of slightly greater diameter than that supplied with the capsule, and applying suction with a 50 ml, instead of a 20 ml, syringe. It is more difficult to judge the exact position of the biopsy head than when using a Wood's tube, which may lead to a few lower oesophageal biopsies being obtained unless x-ray screening is routinely employed.

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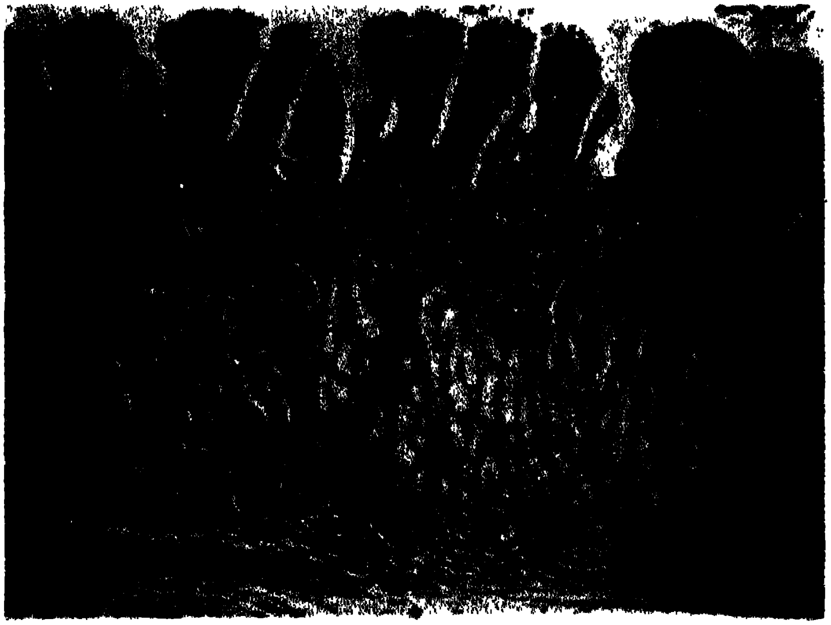
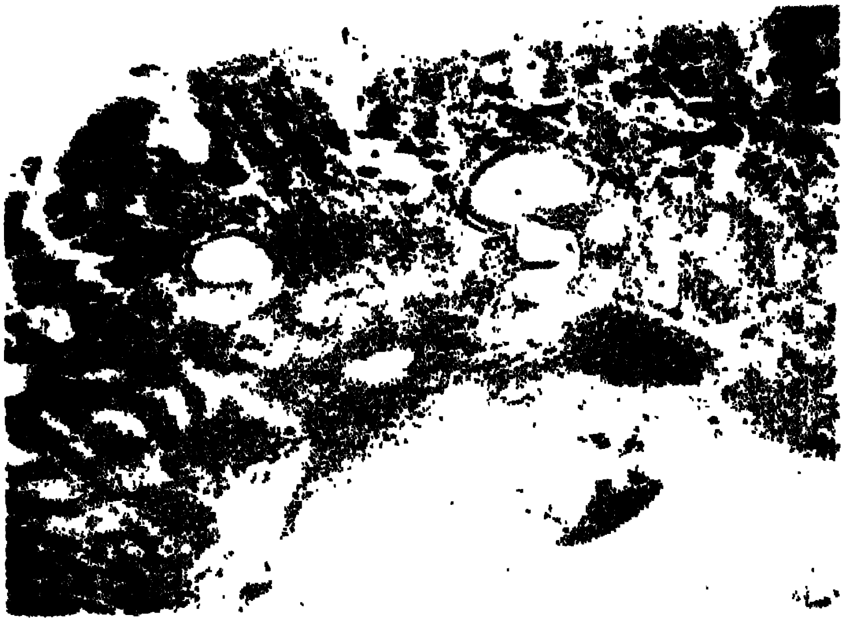
PLATE I



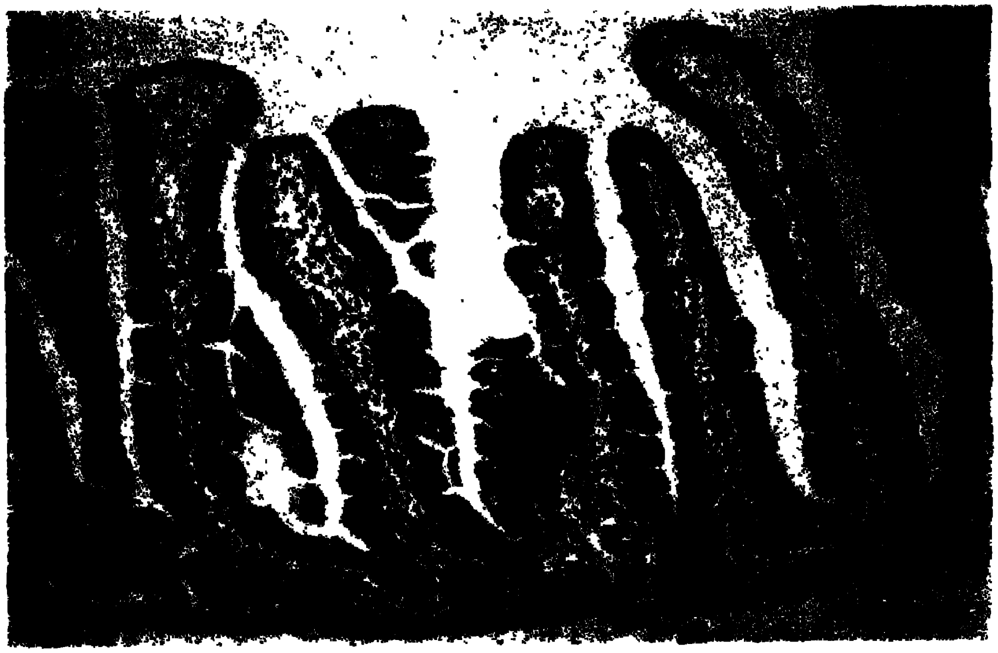
(*a*) *Normal gastric mucosa* × 30. *A thick mucosa with long glands. Under high magnification specific secretory cells can be seen*



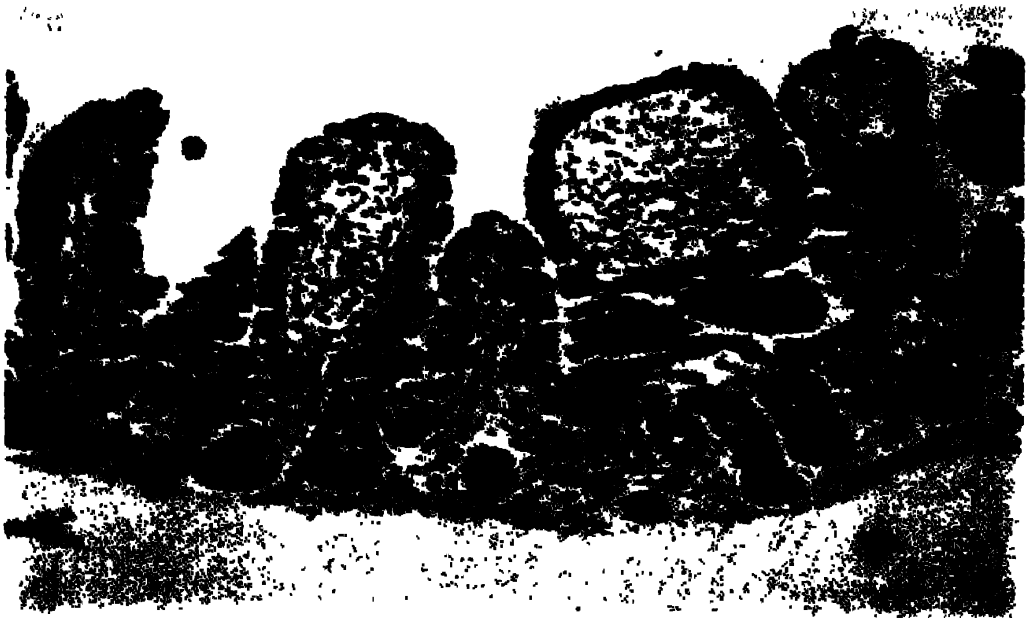
(*b*) *Atrophic gastric mucosa* × 60. *The gastric glandular layer is thin with an inflammatory cellular exudate. There is cystic dilation of many gastric glands and no parietal or chief cells*

[*To face p.* 140

PLATE I



(*c*) *Normal jejunal mucosa* × 60. *A biopsy obtained from a post-gastrectomy patient using a Crosby capsule. Normal long finger-like villi*



(*d*) *Abnormal jejunal mucosa* × 60. *This section was taken from a biopsy from a patient after partial gastrectomy. The patient had iron deficiency, but no other evidence of malabsorption. The villi are irregular and broader than normal; oedema is present*

7

THE EFFECT OF PARTIAL GASTRECTOMY ON THE JEJUNAL MUCOSA

C. Tasman Jones and John A. Williams

Until the introduction of the per-oral biopsy tube there was little opportunity to study the normal human jejunal mucosa. There is extremely rapid post-mortem autolysis of jejunal mucosa, just as there is of gastric mucosa, so that autopsy specimens usually fail to provide acceptable histological material.

Normal Small Bowel Histology

The appearance of the normal small bowel mucosa obtained by the per-oral biopsy has been studied by Baird and Dodge (1957); Shiner (1959); Fone and colleagues (1960) and Girdwood, Delamore and Williams (1961).

When seen under a dissecting microscope, normal jejunal mucosa has long frond-like villi, regular in size and shape. Histological examination of specimens prepared by immediate fixation shows that these villi make up two-thirds of the thickness of the mucosa. At the base of the villi are short depressions, the Crypts of Lieberkuhn, and beneath these is a thin muscularis mucosa. The surface epithelium consists of a single layer of columnar epithelial cells with oval nuclei close to the basement membrane. Interspersed among the columnar cells are goblet cells containing a round mass of mucin. Mitotic activity is common in the crypts, but is not seen in the cells lining the villi. Creamer, Shorter and Bamforth (1961) have shown that there is an extremely rapid turnover of cells in the jejunum, the cell beginning its life at the base of the crypt and migrating towards the tip of the villus whence it is desquamated two or three days later.

Most of the columnar cells are full of granules but, sometimes, large cells containing only scanty granules may be seen. In the crypts are oxyphylic (Paneth) cells and argentaffin (Kultschitzky) cells. The latter are best recognized on sections stained with silver. The stroma of the jejunal mucosa consists of a delicate connective tissue network in which there are capillaries and thin walled lacteals. In the normal mucosa there is usually a moderate infiltration of histiocytes, lymphocytes, plasma cells and eosinophils. Lymphoid follicles, which are common in the duodenum, are found only rarely in the jejunum. There are occasionally ill-defined aggregations of lymphocytes without any evidence of germinal centres (Baird and Dodge, 1957).

In studying sections taken from jejunal biopsies, it is extremely important to ensure that the section has been cut at right angles to the wall of the bowel; a tangentially cut section will make the villi appear short and stumpy, and will give a picture similar to that seen in coeliac disease (Brandborg, Rubin and Quinton, 1959).

CHANGES IN JEJUNAL MUCOSA AFTER PARTIAL GASTRECTOMY

Paulley has put forward the hypothesis that in those cases of post-gastrectomy syndrome in which steatorrhoea develops and the patient loses weight, there may have been latent idiopathic steatorrhoea before operation, the supposition being that the gastrectomy is provocative in pre-disposed subjects by causing unaccustomed conditions in the upper intestine (Paulley, Fairweather and Leeming, 1957). Paulley and his colleagues studied 61 patients admitted for gastrectomy, by means of jejunal mucosal biopsies taken at the time of operation. They describe five in which an abnormal mucosal pattern was found. The abnormality was gross in two and there was steatorrhoea in both of these cases when followed-up after operation; both had a history of bowel disorder before their gastric operation. In the same communication, Paulley describes the case of a man with intermittent diarrhoea and some of the stigmata of 'idiopathic steatorrhoea' who developed gross malnutrition after partial gastrectomy performed for 'duodenal scarring'. Per-oral jejunal biopsy showed a normal mucosa, but after death there were areas of abnormal atrophic jejunal mucosa interspersed with areas of normal mucosa. They suggest that the finding of one normal jejunal biopsy does not necessarily imply that the entire small bowel mucosal pattern is normal. Paulley (1959) again stated that the common finding in the jejunum after gastrectomy is a true atrophy with widely spaced, irregularly shaped villi with crenated borders and pointed tips resembling Christmas trees.

Similar jejunal mucosal changes are reported by Joske and Blackwell (1959). These authors describe thickened, deformed villi with inflammatory infiltration in three out of four cases of post-gastrectomy malabsorption. The villi are described as tapering, but often with a blunt tip. Many of the epithelial cells showed cytoplasmic vacuolation and the goblet cells were more numerous than normal. However, in the two cases in which these changes were most marked there were important complicating factors such as diabetes and rheumatoid arthritis. Systemic lupus erythematosis was not excluded. Some support for Paulley's hypothesis comes from a further case reported by Forshaw (1958), in which malnutrition and impaired nitrogen absorption after gastrectomy was corrected by a gluten-free diet. There is no report of the histological picture of the jejunal mucosa in this case. A gluten-free diet, however, produced no improvement in one of the cases described by Joske and Blackwell (1959).

These isolated reports of abnormal jejunal mucosal patterns, seen in some cases of gross malabsorption after gastrectomy, may represent occasional cases who had coincident idiopathic steatorrhoea and peptic ulceration. It is also of interest to note that in most of the cases showing gross mucosal changes, the operation of partial gastrectomy was performed for a pathological lesion which was not a typical chronic peptic ulcer; for instance, in one of the cases of Joske and Blackwell (1959) who was suffering from rheumatoid arthritis, haematemesis had followed aspirin therapy; and in the case of Paulley and colleagues (1957) there was no frank ulceration at the time of operation. It appears that, in rare instances, patients with mild or latent enteropathy of the gluten sensitivity type develop peptic ulceration and that, in such patients, partial gastrectomy will aggravate their intestinal malabsorption. Such a case is described on page 252. Nevertheless, there are a number of reports of jejunal mucosal biopsies from post-gastrectomy patients, including our own reported below, which do not support Paulley's suggestion that the unmasking of a latent enteropathy is an important cause of post-gastrectomy malnutrition.

Baird and Dodge (1957) reported 31 biopsies of the jejunum taken at intervals after partial gastrectomy; twenty-three of these showed no abnormality. The number and distribution of mucous-containing goblet cells. Paneth cells and Kultschitzky cells did not differ from those seen in the pre-gastrectomy specimens. In four of their cases there was some hyperaemia and oedema of the villi with mild clubbing and intraepithelial oedema. Within these villi were prominent dilated capillaries; they felt that it was not justifiable to label these changes pathological. In two of the 31 cases mild atrophic changes were seen, the villi being short and stubby. Goblet cells were scanty but there was no alteration in the Paneth cells. In one case there was an increase in the cellular content of the mucosal stroma; the infiltration by histiocytes and eosinophils seemed to be much more marked than in the normal specimens; this patient had steatorrhoea. They conclude 'it is clear that in these cases the short circuit had produced no detectable change in the histological appearance of the jejunum'. Shiner (1959) described 15 cases of post-gastrectomy steatorrhoea in which jejunal biopsies were performed. In all but two the biopsies were normal, and in the two abnormal biopsies the changes were not those seen in coeliac disease. In eight post-gastrectomy jejunal biopsies reported by Lees and Grandjean (1958) all the biopsies were normal, except two which showed mild inflammatory changes.

THE AUTHORS' SERIES

Per-oral jejunal biopsies have been obtained by means of a Crosby capsule (Crosby and Kugler, 1957) from 51 patients following partial gastrectomy. In all but four, the operation had resulted in a gastro-jejunal anastomosis. All the specimens were examined under the dissecting microscope and an assessment made of the normality of the villi. The specime and histological section tangential section [see P

On page 144, line 17:
Plate II (*a*) and (*b*) should read Plate I (*c*) and (*d*)

Partial Gastrectomy

Results

The appearances und normal, showing long like villi were seen. This appearance usually corresponded with the histological appearance of villi which were broader and slightly shorter than normal. Such abnormal villi were seen in 10 of the 51 cases. In none of these specimens did we see a flat mucosa with atrophic villi such as that seen in cases of coeliac disease (Fone and colleagues, 1960; Girdwood, Delamore and Williams, 1961). In all the cases where there appeared to be some abnormality of villus shape the individual cells were normal with a normal brush border.

Distinct oedema of the villi was seen in three specimens. In two of these the villi were of the short stubby type but in the other one the villi were of normal length. An abnormally heavy infiltration with inflammatory cells was seen in only one biopsy and in this the villi were normal and there was little oedema. This last case had both iron and vitamin B_{12} deficiency. Some cellular infiltration was seen in all but three of the biopsy specimens in common with the finding in many normal operative control biopsies. We found no correlation between the jejunal biopsy findings and the presence or absence of anaemia, of increased frequency of bowel action or the loss of weight. No pathological changes were found in the four jejunal biopsies taken after operation with a gastro-duodenal anastomosis. Our findings were in keeping with those of Baird and Dodge (1957).

It is possible that cases with a patchy jejunitis (Paulley, Fairweather and Leeming, 1957) may not have been detected by the biopsy. In five cases more than one biopsy specimen was obtained and, in these, no evidence of any significant dissimilarity was seen.

MILK INTOLERANCE OR MILK SENSITIVITY?

For many years there have been reports in the German and French literature referring to milk intolerance developing after partial gastrectomy. Hoffman (1939a, 1939b and 1952) reported that 5 10 years after Billroth II gastrectomy, 62 per cent of patients had mild or moderate post-cibal symptoms, one of the most common of which was discomfort following drinking raw milk. Similar findings were reported by van Goidsenhoven and colleagues (1946); Brun and Landelius (1947); Gaviser (1948); Bernay and Blanchet (1950); and Pfisterer (1951). These reports were summarized by Meurling (1953), who suggested that a true allergy to milk might be responsible for the milk intolerance syndrome. He stated that post-cibal symptoms after gastrectomy were worse in people with a history of allergic phenomena (asthma, eczema, hay fever). In a series of 624 patients reviewed after partial gastrectomy, he found that 47 per cent had at some time noticed an intolerance to milk products.

Milk intolerance after gastrectomy may be due, in part, to the physical effects of the liquid milk. In the normal alimentary tract milk is clotted into a semi-solid bolus in the fundus and only passes through into the duodenum after it has been rendered more nearly isotonic and isothermic. After gastrectomy, milk may not be clotted in the stomach but poured directly into the jejunum, where it stimulates peristalsis and rapidly passes through the small bowel.

It has been claimed that 'dumping' may be induced by raw milk (Bernay and Blanchet, 1950; Pfisterer, 1951) but this is unlikely since the dumping syndrome is induced by the intrajejunal dumping of hypertonic solutions (see p. 70) (Machella, 1950; Glazebrook and Welbourn, 1952; Le Quesne, Hobsley and Hand, 1960) and milk is hypotonic or nearly isotonic. We have measured one sample of raw milk which had an osmolarity of 238 milliosmoles/litre.

We have seen many patients who profess intolerance to milk which developed after partial gastrectomy. In three of these the withdrawal of milk from their diet resulted in a striking improvement in post-cibal discomfort and diarrhoea. In one of the three the jejunal mucosa was examined by per-oral biopsy and was normal.

SUMMARY

Our findings confirm the impression of Baird and Dodge (1957) and Clark, Williams and Scott (1963), that (there is no consistent histological change in the jejunal mucosa after gastrectomy. Alterations in the structure of jejunal mucosa are therefore probably not an important cause of malabsorption of iron or fats in post-gastrectomy patients.)

(Intolerance to milk which often occurs after gastrectomy is not an example of the true 'dumping syndrome', neither does it appear to be an example of true 'sensitivity'.)

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8

ANAEMIA AND THE POST-GASTRECTOMY STATE

Eric V. Cox, John A. Williams and C. Tasman Jones

Anaemia is the result in a reduction of the normal red blood cell count or haemoglobin content, or both, in the peripheral blood. Fundamentally, it results from increased haemolysis, blood loss or disordered red cell production by the bone marrow. Nearly all instances of anaemia resulting from gastric operations are accounted for by blood loss and by disordered erythropoiesis due to deficiencies of iron, vitamin B_{12} and, occasionally, folic acid. Other factors which can produce anaemia may occasionally occur after partial gastrectomy, as, for example, infection of a 'blind' afferent loop. It is not the point of this chapter to discuss the whole field of haematology since any type of anaemia may occur in patients having had a partial gastrectomy. Discussion is limited to those conditions which might be directly associated with successful gastric surgery. Thus, the haematological effects of obvious recurrences of peptic ulceration or neoplasia are omitted.

The *classification* of anaemia based on red cell morphology is of limited value only, although it does serve to delineate three overlapping groups:

(1) Macrocytic anaemia due to deficiency of vitamin B_{12}, or folic acid, is usually characterized by an abnormal or megaloblastic type of red cell formation in the bone marrow. The bone marrow changes may be difficult to determine in patients with minimal degrees of anaemia.

(2) Microcytic or hypochromic anaemia in nearly every instance is due to iron deficiency. The red cell count is not less than 3·5 million/ml, and the erythropoiesis is normal.

(3) Normocytic, normochromic anaemia most commonly results from fairly acute blood loss and resultant haemo-dilution. The bone marrow shows a normal or normoblastic erythropoiesis, although this may be hyper-active.

Following partial gastrectomy, disturbances of vitamin B_{12} and iron metabolism are not uncommon, as will be seen, so that if they occurred later, the findings in the peripheral blood may present a mixed picture making the initial classification of the patients difficult. Also, the degree of the deficiencies may be sufficient to produce symptoms while the patient's blood picture remains within the normal range. The appropriate therapy will, however, produce symptomatic improvement and also prevent those rare occurrences of severe disorders which can even occur in the pre-anaemic state, such as sub-acute combined degeneration of the cord, depressive states, convulsions and optic atrophy.

Anaemia is probably the most common complication of partial gastrectomy. During the past seven years we have studied over 250 cases in detail. Many of these patients were assessed haematologically before operation, and at a minimum of six-monthly intervals thereafter; others were studied because they had developed clinical anaemia; and a group of 100 unselected patients was examined as an investigative project 5-6 years after gastric operations. Observations on these patients provide the basis for this chapter.

THE INCIDENCE OF ANAEMIA

Deller and Witts (1962) analysed 33 reports comprising 7,505 patients who had undergone partial gastrectomy and calculated that anaemia was present in 28 per cent. However, the incidence shows wide variations in the different series, and this has been largely explained by the differences in the criteria adopted for the diagnosis of anaemia, and the thoroughness of the haematological investigation, and also by the proportions of men and women in the series, the indications for operation, the type of operation performed and the period of observation following operation.

The estimation of haemoglobin in the peripheral blood, because of its simplicity, has become the yardstick for the presence or absence of anaemia. Some authors maintain that anaemia is present only if the haemoglobin level is below 12·5 g per cent. Others set the lower limit of normal as 13·8 g per cent for men and 11·97 g per cent for women (Wintrobe and White, 1940), while Baird, Blackburn and Wilson (1959) defined anaemia as a haemoglobin level below 13·3 g per cent in men and 10·4 g per cent in women. Since the degree of anaemia in the post-gastrectomy state is usually slight, it is easy to understand how different criteria of assessment may affect the alleged incidence of deficiencies.

The object of any haematological investigation is not so much to determine an increased incidence of abnormalities in one or other sex or after different operations, as to detect deficiency states in individual patients. Too frequently—and of necessity from the point of view of writing papers—the emphasis is on the former, and apparent minor haemotological changes have, as a result, been ignored by the clinician. The correction of these borderline deficiencies will, however, improve the patient's well being. In order to detect these borderline cases a full haemotological investigation is essential. For example, a normal red cell count, associated with haemoglobin levels just above the postulated lower limits of normality would be indicative of hypochromia, whereas a normal haemoglobin level with a reduction of the red cell count may indicate hyperchromia and macrocytosis. Some examples of this occurrence are given in Table 6 and illustrate the importance of carrying out both red cell counts and packed cell volume determinations. Normal blood values as determined by Dacie (1950) are included in Table 6, and we feel that patients with partial gastrectomy who do not satisfy all these criteria should be investigated further for an underlying deficiency state.

In our series of 100 patients examined 5–6 years after gastric operations (Jones and colleagues, 1962), 55 had an abnormal blood picture. Using the criteria of Baird, Blackburn and Wilson (1959) for the presence of anaemia, 23 were anaemic, of whom 5 were microcytic, 16 normocytic and 2 macrocytic; 14 other patients had a macrocytosis, and a further 18 had a reduced mean corpuscular haemoglobin concentration.

IRON DEFICIENCY

The most frequently recognized type of anaemia following partial gastrectomy is that due to iron deficiency, as judged by the serum iron levels, the appearance of the bone marrow and the response to iron therapy (Lyngar, 1950). Watson (1947) reviewed 132 cases after Billroth II gastrectomy and found 17 cases of anaemia (as judged by haemoglobin levels below 13·8 g/100 ml in men and 11·7 g/100 ml in women). He noted that anaemia was more common three or more years after operation (18 per cent) than it was less than three years after (7·7 per cent). It was twice as common in women (20 per cent) as in men (9·3 per cent). Anaemia was commonly found in patients who had low haemoglobin levels prior to operation, and it was more common in patients who had had operation for gastric ulcer than in those who had had operation for duodenal ulcer. More recently Baird, Blackburn and Wilson (1959), using the criteria described on page 149, found anaemia in 41 cases out of 341 patients studied at various intervals after different types of partial gastrectomy for duodenal or gastric ulceration. In all but one of

TABLE 6

All Patients Have 'Normal' Haemoglobin Levels. Patients 1–5 Have Increased Mean Corpuscular Volumes (M.C.V.) and Low Serum Vitamin B_{12} Levels. Patients 6–8 Have Subnormal Mean Corpuscular Haemoglobin Concentration Levels (M.C.H.C.), Low Serum Iron (Serum Fe) and Raised Total Iron Binding Capacity Levels (T.I.B.C.). Patient 9 Has Low Iron and Vitamin B_{12} Levels, a Raised T.I.B.C. and Hypochromia (Low M.C.H.C.)

Patient	*Sex*	*Age*	*R.B.C.* million	*Hb* g per cent	*P.C.V.* per cent	*M.C.V.* μ^3	*M.C.H.C.* per cent	*Serum* B_{12} $\mu\mu g/ml$	*Serum* Fe μg per cent	*T.I.B.C.* μg per cent	*Remarks*
Normal values	M F		4·5–6·5 3·9–5·5	13·5–18·0 11·5–16·4	40–54 36–47	76–96	32–36	140 to over 500	40–160	250–420	
1	M	48	4·06	15·8	47	**116**	33·5	**50**	210	380	Vitamin B_{12} deficiency with macrocytosis
2	M	60	4·33	14·0	43	**100**	32·5	**110**	50	**441**	
3	F	68	4·28	14·5	44	**102**	33·5	**110**	58	343	
4	F	61	3·92	14·0	41	**104**	34	**65**	61	**550**	
5	F	45	3·79	13·0	41	**108**	32	**25**	63	320	
6	F	57	4·76	12·8	41·5	87	**31**	165	**30**	**547**	Iron deficiency with hypochromia
7	M	49	5·16	13·9	45·5	88	**31**	195	**24**	**485**	
8	F	61	5·30	12·5	42	78	**30**	230	**27**	**457**	
9	F	67	5·30	13·1	42	79	**31·5**	**65**	**31**	**520**	Iron and B_{12} deficiency

Note.—Abnormal values are given in bold type.

their patients, as also in all but one of the series of Watson, the blood findings indicated that the anaemia was of the iron deficiency type. While an incidence of anaemia varying from 0 to 60 per cent is reported in different series, all agree that the anaemia is predominantly of the iron deficiency type, and the majority state that the incidence increases with the passage of time after operation.

TABLE 7

Author	*Year of publication*	*No. of cases*	*Type of operation*	*Incidence of anaemia* per cent	
				Women	*Men*
Larsen	1934	86	Not stated	48·5	27·4
Bruusgaard	1946	Under 40 years old 155	Billroth II	59·1	26·1
		Over 40 years old—137	Billroth II	28·7	31·1
Watson	1947	132	Billroth II	20	9·3
Ramberg	1948	203	Not stated	25	19
Gaviser	1948	416	Billroth II	17	0
Drablos, Linden and Skjelbred	1951	313	Billroth II	41	26

It is usually stated that iron deficiency anaemia is more common in women than in men but, as we have stated, the incidence will depend on whether the lower limit of haemoglobin which is normal for women is taken as being 12·5, 11·7, 11·5 or 10·4 g/100 ml. Table 7 shows the incidence of anaemia in a number of reported series. In the 234 patients reviewed by Baird, Blackburn and Wilson (1959), where the lowest of the normal haemoglobin ranges was used, there is no significant difference in the incidence of anaemia between women and men. It is evident that the low haemoglobin levels found in younger women after gastrectomy is due to their low pre-operative iron stores and to their increased post-operative iron losses in menstruation and pregnancy.

(Anaemia has been reported to be more common after Billroth II than after Billroth I operation)(Morley and Roberts, 1928) but this observation depends on a number of factors. The influence of sex has already been mentioned. Watson (1947) found that anaemia was more common after partial gastrectomy for gastric than for duodenal ulceration, and all his patients had had the Billroth II type of operation. Since it is common practice to perform a Billroth I operation for gastric ulcer and a Billroth II for duodenal, the resultant comparisons of the two operations will be difficult (or impossible) to interpret. For example, in our own series (Jones and colleagues, 1962) 24 patients had a Billroth I operation for gastric ulcer and 57 a Billroth II operation for duodenal ulcer. Five years later we were unable to find any significant difference in the haemoglobin levels in the two groups.

It is obvious that, in order to compare the effect of the two types of operation on the incidence of anaemia, a series must be studied in which groups comparable by age and sex, with comparable iron reserves, are operated on by the same surgeons who removed the same measured amount of stomach from the patients in each group and, by random selection, perform either a gastro-duodenal or gastro-jejunal reconstruction. The groups must then be followed-up for the same time period after operation, ensuring that neither group is given oral iron therapy and that the incidence of anaemia be determined by the same criteria. As far as we are aware, no such study has been reported and, therefore, we must conclude that there is no unequivocal evidence that the type of operation affects the incidence of iron deficiency anaemia. We have seen examples of iron deficiency after every type of operation for peptic ulcer, including vagotomy plus antrectomy, and vagotomy plus gastro-enterostomy. We have not seen any cases of iron deficiency after vagotomy plus pyloroplasty, but we have so far seen very few of these patients more than five years after operation.

However, we have studied 28 patients who had duodenal ulcer which was successfully treated 14–15 years ago by vagotomy without the addition of drainage procedure. All but two of these were known to have complete vagotomies judged by the insulin test (Hollander, 1946); the other two were presumed to be complete. In none of these 28 patients was there any detectable anaemia (see Chapter 11, p. 271). Unfortunately, vagotomy alone is not a satisfactory operation because of the prohibitively high recurrence or gastric ulcer rate (Slaney, Bevan and Brooke, 1956).

Thus we conclude that iron deficiency is common in both men and women following partial gastrectomy or gastro-enterostomy, but that available data suggest that the incidence is less in patients who have had vagotomy alone or combined with pyloroplasty.

Aetiology of Iron Deficiency

Dietary Deficiency.—Hartfall (1934) stressed the importance of dietary factors in the aetiology of post-gastrectomy anaemia. He was impressed by the frequency of poor diets among his anaemic patients. Unfortunately, dietary histories are often extremely unreliable. In our experience, under the improved social conditions of 25 years later, we have found no evidence that the quality of the diet of post-gastrectomy patients is deficient in iron-containing foods. However, following gastrectomy, many patients reduce their total intake of food, and although the diet may be qualitatively adequate, their actual intake of iron-containing foods may be quantitatively sub-optimal. Furthermore, epigastric fullness after meals frequently accompanies iron deficiency, so that the anorexia could be a result of the deficiency rather than the cause. It must not be forgotten that recurrent ulceration can produce both anorexia and blood loss.

We feel, therefore, that although dietary deficiency may be of prime importance in the occasional case of iron deficiency following a gastric operation, it is only a supplementary or secondary factor in the majority of patients.

Impaired Iron Absorption.—In man the daily absorption from a diet containing 15 mg of iron is 1–2 mg, i.e. 7–15 per cent, which just balances the daily loss of iron, including that lost by women in menstruation. In iron deficiency anaemia, absorption is increased and may rise to 30 per cent of the daily intake. The controlling factors in this delicate balance have not been completely elucidated. It is generally believed that iron absorption is impaired after partial gastrectomy, but conclusive evidence for this belief is not available despite many experimental studies. Some of the sequelae of gastrectomy which may interfere with iron absorption are as follows.

(1) *Hypochlorhydria*. For normal iron absorption, the amount of iron available in a soluble ferrous state in the duodenum is important. This amount might be reduced by the hypochlorhydria which is the sequel and, indeed, the object of gastric operations. This hypothesis is supported by the experimental work of Choudhury and Williams (1959), who showed a reduced ability to absorb ferric iron incorporated in bread in patients after partial gastrectomy. Despite these theoretical disadvantages of hypochlorhydria, it has been shown that complete achlorhydria does not necessarily prevent the absorption of iron either from foodstuffs or from therapeutically administered salts (Davidson and Markson, 1955; Moore and Dubach, 1956; Badenoch, Evans and Richards, 1957).

(2) *Rapid Gastric Emptying.* The stomach has an important role in regulating the delivery of food into the small intestine so that maximum digestion and absorption may take place, a mechanism which will naturally be disturbed by a gastro-enterostomy, antrectomy and, probably to a lesser extent, by pyloroplasty (see Chapters 5 and 11). It has been suggested that the loss of this mechanism may adversely affect iron absorption (Owren 1952; Witts, 1956; Wallensten, 1958).

(3) *Duodenal By-pass.* Evidence has accumulated which indicates that the proximal small intestine is the main site of iron absorption (Hahn and colleagues, 1943; Endicott and colleagues, 1949; Stewart and colleagues, 1950; Witts, 1956). This provides a theoretical basis for malabsorption of iron following gastro-enterostomy and the Billroth II type of gastrectomy.

However, despite these theoretical implications, Baird and Wilson (1959) found no impairment of the absorption of radioactive ferrous sulphate given in a fasting state, or of radioactive iron incorporated into rabbits' blood and given with a light meal to patients with partial gastrectomy. On the other hand, these factors are probably of importance in the further observation of Baird and Wilson, that iron deficient gastrectomized patients showed only a slightly enhanced absorption, compared with the increase of up to four times that which occurs in patients with iron deficiency who have intact stomachs. Choudhury and Williams (1959) also found that, in anaemic patients after partial gastrectomy, especially of the Billroth II type, the absorption of radioactive iron in a ferric state incorporated into bread was reduced.

Thus, it appears that in the majority of instances of iron deficiency following partial gastrectomy, malabsorption of iron at normal levels is not an initiating factor, although it may supplement a reduced dietary intake or potentiate iron deficiency due to slight or intermittent blood loss. In other words, if, after gastrectomy, occult or overt bleeding occurs, there is a reduced ability to increase iron absorption to replete the losses. It is not clear whether this inability to increase iron absorption to meet increased needs is due to hypo-acidity or rapid passage through, or by-passing of, the duodenum, or to a combination of these and other factors. However, it would certainly appear that the defect is predominantly in the release of iron for absorption, since inorganic ferrous iron will, in most instances, correct a deficiency when given by mouth.

The State of Iron Saturation at the Time of Operation. Bleeding from the ulcer, for which the operation was performed, naturally depletes the body iron stores. This may be recognized from a history of haematemesis or melaena, but more often it is occult. By the time that such a patient develops iron deficiency anaemia, the body iron stores are exhausted, so that a patient coming to operation without frank anaemia may, nevertheless, have little or no reserve of iron; the anaemic patient certainly has none.

The total body stores of iron amount to 4·5 g, of which only 2·5 g is present in the haemoglobin, so that an anaemic ulcer patient coming to operation may have his haemoglobin level raised by transfusion to normal levels, and yet remain with depleted iron stores.

Usually, surgeons would be unwilling to operate on a patient with a haemoglobin below 70 per cent (10 g/100 ml), yet it is not generally realized that if a partial gastrectomy is performed on a patient with a haemoglobin of 80–90 per cent who, at the same time, appears to have depleted iron stores, that patient is unlikely to be able to replete his iron stores without supplementary iron therapy.

Operative Blood Loss.—The quantity of blood lost during operation is a significant factor in patients such as we have just described. Surgeons have an invariable and understandable tendency to underestimate the blood loss at operation, a fact observed by Coller and Maddock (1932). In consequence, many may feel that a blood transfusion during a gastrectomy reflects adversely on their surgical skill. Many careful studies in more recent years have shown that in almost any operation of the magnitude of a partial gastrectomy, and performed by surgeons deliberately attempting to minimize bleeding, the measured blood loss was in the region of 750–1,000 ml (Coller, Cook and Iob, 1944; Bonica and Lyter, 1951; Williams and Parsons, 1958). Hercus and colleagues (1961), using the method of swab weighing to determine blood loss, reported 13 operations of partial gastrectomy in which the blood loss varied from 200 to 1,800 ml (mean 700 ml). Swab weighing tends to underestimate blood loss. Rains (1955), using the method of weighing the patient, which also measures fluid loss by evaporation, found that the loss was 450–650 ml for a simple gastrectomy, but as high as 1,450–1,950 ml when a radical operation was performed for carcinoma, or a revision gastrectomy for gastro-colic fistula.

When replacing blood lost at operation, it must be remembered that one bottle (540 ml) contains only 420 ml of whole blood, the remaining 120 ml being citrate solution. When the bottle, and particularly when the tubing, is changed a further 20–50 ml of blood is lost and, as Rains (1955) pointed out, one finds that just over half a pint of blood has in fact been given when one imagines that a whole pint has been given. Therefore, from the point of view of preventing loss of iron as well as of minimizing the ill-effects of the operation, any patient who has a gastrectomy may need 2–5 bottles of whole blood.

A patient who loses 1,000 ml of blood during a mastectomy can quickly make good the deficit by absorbing rapidly from the diet the equivalent of the lost iron, but a patient losing a similar quantity during gastrectomy is less able to repair the deficit.

Post-operative Blood Loss—The causes of immediate post-operative bleeding are discussed in Chapter 3; they include continued bleeding from an ulcer not removed by the operation, or from the suture line at the anastomosis, or continued oozing of blood from the gastric mucosa. Paulson and Harvey (1954) and Witts (1956) suggest that the rapid appearance of anaemia, which is occasionally encountered after operation, can only be accounted for by active haemorrhage.

Chronic or intermittent blood loss may result from reflux oesophagitis, recurrent ulceration or, where there is a gastro-jejunostomy, jejunitis or gastric stomatitis. All these are possible complications of partial gastrectomy. Baird, Blackburn and Wilson (1959) observed that up to 6 per cent of their patients with partial gastrectomy had occult blood in the faeces as revealed by the benzidine test. Tests for occult blood in the stools were negative in the majority of the patients whom we have observed with iron deficiency after gastrectomy. These negative results indicated only the absence of fairly gross bleeding (over 20 ml at a time) and, as we employed 'haematest' tablets on ambulent out-patients without dietary restriction, the tests were not so delicate. It must also be realized that with a haemoglobin level of 50 per cent, the blood loss would need to be 40 ml to be detected by this method. In order to determine whether losses of small quantities (5–10 ml) of blood were occurring, it is necessary to restrict the patients to a strict meat-free diet and to ensure that they avoid brushing the teeth for 2–3 days before examining the stool for blood with the orthotoluene test or with 'occultest' tablets.

Without such precautions a high proportion of false positive reactions are obtained, thereby making the results unreliable. In a small number of in-patients in this iron deficiency group whose stools were examined for 5–7 days by the more sensitive method, we still failed to demonstrate the presence of occult bleeding.

This does not rule out the possibility of blood loss, for we are all aware of the rapidity with which the occult blood test can become negative after acute gastro-intestinal haemorrhage. Intermittent blood loss from superficial erosions in the oesophagus, stomach, duodenum or jejunum causing blood loss of a lesser degree, say equivalent to 20 ml of blood per week, would increase the daily requirement of iron by 1 mg/day or 50 per cent (20 ml of normal blood contains approximately 8 mg iron). In other cases a blood loss of, say, 100 ml occurring on only one day in a month, with negative occult blood tests for the remainder of the month, could account for the gradual onset of iron deficiency when associated with the inability of gastrectomized patients to increase their iron absorption.

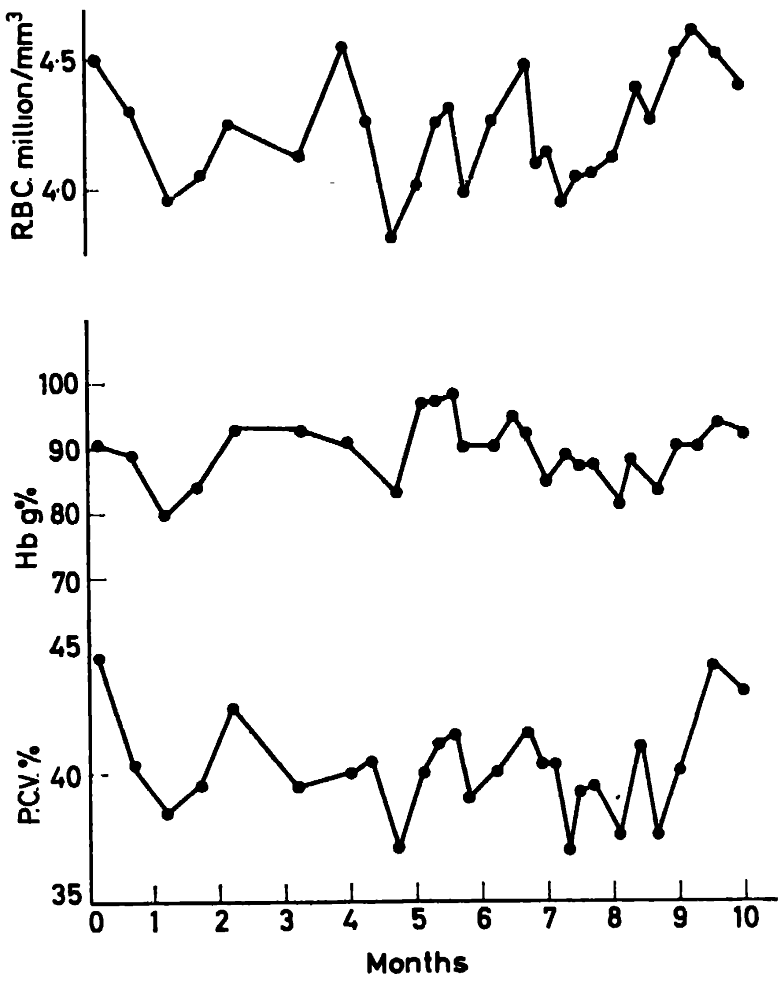

Figure 39. Fluctuations of haematological indices in a male patient with a Billroth II gastrectomy. During the whole of the ten-month period he was receiving daily oral iron and weekly injections of vitamin B_{12}. The fluctuations are almost certainly due to intermittent blood loss despite repeatedly negative tests for blood in the stools

In post-gastrectomy patients observed regularly for a number of years, fluctuations in the peripheral blood picture and the serum iron levels are often of such a magnitude as to be inexplicable by any other cause than blood loss (an example is shown in *Figure 39*).

Another important cause of blood loss from the alimentary tract is the taking of aspirin in any form. As Kay (1962) has shown, healthy young adults taking 2 g of aspirin per day, irrespective of the way it is dispensed, will invariably have detectable blood in their stools. Increased losses of iron from this cause may be significant in a person who, by surgical intervention, has been rendered incapable of increasing iron absorption above the minimum requirements. The same effect will be observed when the iron loss is not from the upper gastro-intestinal tract, as in haemorrhoidal bleeding, menorrhagia or even epistaxes.

The Clinical Picture of Iron Deficiency Following Partial Gastrectomy

In patients with the classical features of iron deficiency the clinical picture is easily recognized. The symptoms of anaemia, including dyspnoea and lethargy, may be associated with the classical signs of pallor, dryness of the skin, koilonychia and angular stomatitis. In the post-gastrectomized state the clinical picture is not infrequently coloured by other consequences of the operation, such as anorexia, epigastric fullness after meals and weight loss.

However, the degree of anaemia, as judged by the haemoglobin level, is usually slight and the classical signs are relatively infrequent. Mild apathy, anorexia, lethargy with epigastric discomfort and weight loss, are the commonest presenting symptoms. The vague nature of the malaise, and 'normal' or near normal haemoglobin estimation, have rendered some patients liable to be labelled psychoneurotic.

Since we began reviewing post-gastrectomy patients who have not been seen at hospital for five or more years since their operation, we have been impressed by the large number who have not even considered consulting their general practitioners, although they had symptoms which responded dramatically to iron therapy. Usually, they did not seek advice because the symptoms were insidious in onset, and were attributed by the patient to their age or were accepted as an inevitable result of a major operation. As the symptoms are only revealed by direct questioning they are liable to be overlooked at routine review, particularly when the operation has relieved the patient of the more severe symptoms of peptic ulceration.

It is in this type of patient, also, that an estimation of the haemoglobin level alone is of little use. Some of the patients with 'normal' haemoglobin levels will, however, have a mean corpuscular volume below 76 μ^3 and others a mean corpuscular haemoglobin concentration below 32 per cent, both indications of an iron deficiency. A number of patients whom we have observed at frequent intervals from the time of operation have developed symptoms of iron deficiency when their blood picture was still within the normal range, although it had fallen significantly from their own normal levels as observed in the pre- and immediate post-operative periods (*Figure 40* shows such an example). This patient had a minimum red cell count of 5·2 million/ml and haemoglobin of at least 14·6 g during a three-year period following gastrectomy. During the following four months these levels fell to 4·6 million/ml and 13·8 g (still well within the normal range), during which time he developed lethargy, anorexia, and lost 7 lb. in weight. During the following three months, iron therapy corrected his symptoms and peripheral blood findings, and his weight returned to normal.

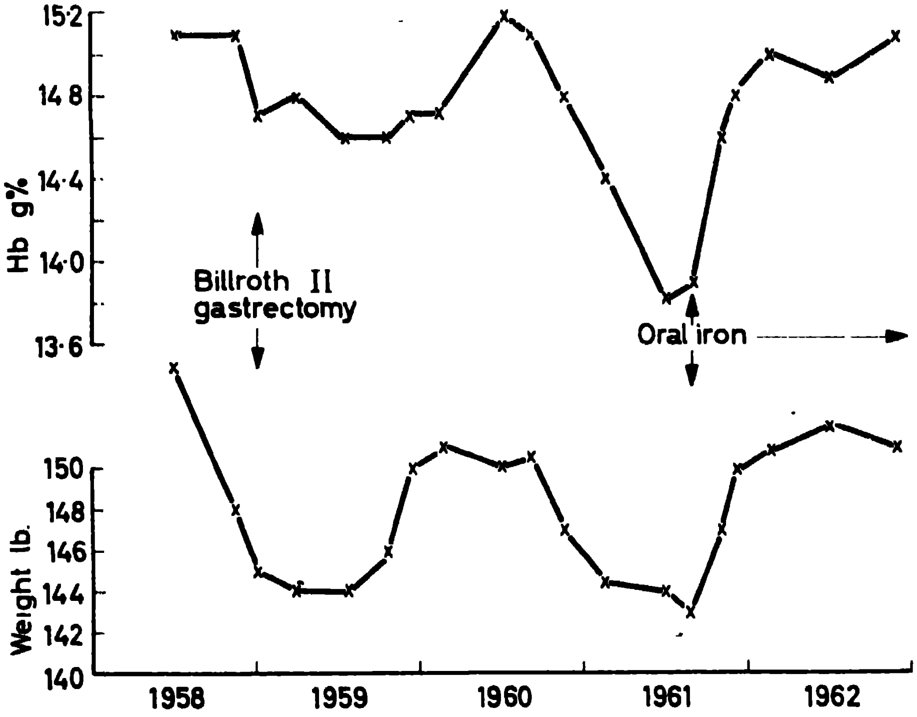

Figure 40. Changes in weight and haemoglobin in a patient following Billroth II type partial gastrectomy with a response to iron therapy. The haemoglobin level never fell below the normal range

In patients with chronic iron deficiency, the serum iron level is usually below 40 mg/100 ml; however, there is now evidence to suggest that chronic deficiency states may occur in patients with serum iron levels in the normal or low normal range.

A few years ago it would have been haematological heresy to say that iron deficiency could be diagnosed in the presence of a 'normal' haemoglobin level and a normal serum iron concentration.

(The classical view was that, as a result of iron deficiency, the iron stores become depleted first, then the haemoglobin and, lastly, the iron-containing enzymes.) Beutler (1957) has challenged this view and has shown that, in animals which have been bled to render them iron deficient, certain iron-containing enzymes can be grossly reduced in their tissues, yet the haemoglobin level still remains within the normal range. In a double blind trial he has also observed the beneficial effect of iron therapy in a series of patients (not post-gastrectomy) with iron deficiency symptoms and no apparent anaemia (Beutler, Larsh and Gurney, 1960). Furthermore, Wallensten (1955) has shown an increase in well-being, improvement in appetite and disappearance of upper abdominal symptoms following iron therapy in partially gastrectomized patients with 'normal' haemoglobin levels. Our own observation strongly supports Wallensten's findings.

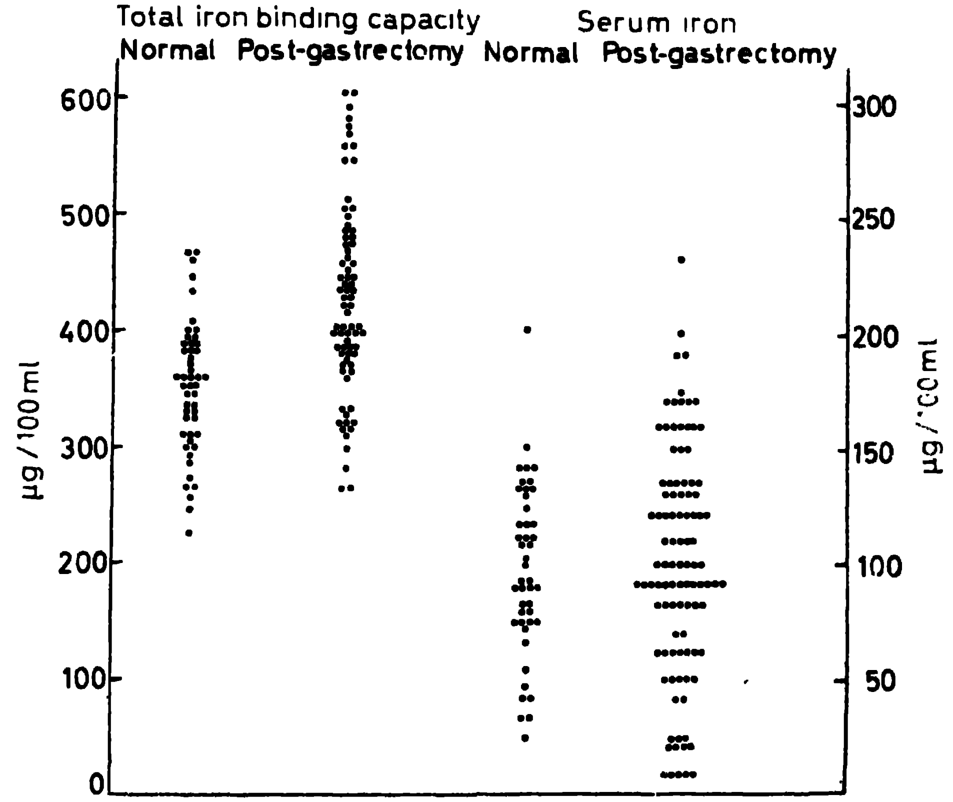

Figure 41. The distribution of the serum iron and total iron binding capacity levels of 100 unselected patients 5–6 years after partial gastrectomy compared with normal controls

In our series of 100 cases, low serum iron levels (below 40 µg/100 ml) were found in 12 patients, but abnormally high levels of the iron binding capacity (above 420 µg/100 ml) were found in 36 patients. A comparison of the distribution of these two determinations is shown in *Figure 41.*

We suggest that, even in the presence of normal serum iron and haemoglobin levels, an elevation of the total iron binding capacity is evidence of established or impending iron deficiency. This opinion is based on observations before and after a three-month course of oral iron in patients who would not generally be classified as anaemic or iron deficient. The response to iron therapy indicates that initially, there was an iron deficiency. An example is given in Table 8.

TABLE 8

A Lady of 56—Six Years After a Billroth II Operation for Duodenal Ulcer

	Hb g per cent	*P.C.V.* per cent	*M.C.V.* μ^3	*M.C.H.C.* per cent	*Serum* B_{12} $\mu\mu g/ml$	*Fe* $\mu g/100\,ml$	*T.I.B.C.* $\mu g/100\,ml$
Before iron	12·7	40·5	85	31·0	144	66	545
After 3/12 iron	14·0	41·0	87	34·5	140	156	475

The Investigation of Iron Deficiency Following Gastric Operations

The Detection of Iron Deficiency—In summarizing the preceding sections, it may be said that, after partial gastrectomy, iron deficiency should always be suspected. Classical physical signs are usually absent and the symptoms are often vague and minimal. The most valuable method of early detection is through a regular estimation of haemoglobin and standard blood indices. For this reason it is always worth while obtaining an estimation of the patient's blood values during the post-operative period immediately after a three-month course of oral iron. Thus a base line is established, against which the earliest signs of hypochromia or microcytosis can be judged. Confirmation of iron deficiency may be obtained by finding a low serum iron level (below 40 μg/100 ml) or, in our opinion a more sensitive guide, a high total iron binding capacity (above 420 μg/100 ml).

If there is still doubt about the presence of iron deficiency in suspicious cases the subjective response to a course of iron therapy, combined with the objective measurement of increase in weight and the reversal of any haematological trend towards hypochromia or microcytosis, is usually confirmatory.

The Source of Iron Losses—The history may provide evidence of obvious abnormal losses of blood, such as epistaxis, menorrhagia or piles. It is important to bear in mind losses which may occur from oesophagitis and to enquire whether the patient is taking any drugs, particularly those containing aspirin. Where there is a history of haematemesis or melaena a full gastro-intestinal investigation, including radiology and gastroscopy, is mandatory. Gross hypochromic anaemia or persistently positive reactions of the stool to 'haematest' tablets also necessitates investigation to exclude recurrent peptic ulceration. In our experience of post-gastrectomy anaemia it is uncommon to find any obvious pathological lesion, such as stomal ulceration, gastric stump carcinoma or reflux oesophagitis, although we have seen isolated cases of anaemia from each of these causes. In a few anaemic patients we have found, on peroral biopsy or gastroscopy, evidence of inflammation or erosion of the stoma itself, or the jejunum beyond. In general, however, we have found no co-relation between the jejunal biopsy appearances and the presence of anaemia (Jones and colleagues, 1962).

Treatment of Iron Deficiency—The prevention of iron deficiency after gastric operations is obviously the ideal; this is simple and practical in most cases. The first step is to replenish the body iron stores. At present there is no simple method available for the estimation of the body iron stores, so that, in practice, the best policy is to assume that all patients with chronic peptic ulcer who require operation are, to some extent, iron deficient. At the time of decision to use surgical treatment, iron therapy is commenced and continued up to the time of operation and for three months afterwards. This is a safe, simple and cheap precaution, and one which is usually well tolerated by patients with peptic ulceration, provided the dose of iron is no more than 200 mg of ferrous sulphate, or the equivalent, three times per day.

This counsel of perfection is not possible when some complication of the peptic ulceration dictates immediate or early surgical intervention, but it is worthy of serious consideration before a premeditated operation. At least we should ensure that anaemia is corrected, and that iron lost at operation is made good. Our practice is to prescribe ferrous sulphate (200 mg) or ferrous gluconate (300 mg), together with ascorbic acid (200 mg), three times a day after meals. The administration of ascorbic acid lessens the incidence of intolerance to iron therapy and its reducing properties are known to assist iron absorption. The maintenance of normal haemoglobin and normal iron stores is usually achieved by prescribing a yearly course of one month's treatment with iron and vitamin C in the same dosage as in the immediate post-operative period. The patient is often the best person to entrust with the responsibility of remembering the yearly iron replenishment. We suggest, however, that all patients after partial gastrectomy should be reviewed each year, ideally by their general practitioner, and that at this visit iron therapy for one month could be arranged.

Only under exceptional circumstances should a patient who has had a partial gastrectomy donate blood. However fit the patient may be after gastrectomy, and however high the haemoglobin level, it is unwise to deplete the iron stores when the patient's ability to replace them is diminished. If it is essential for blood to be taken from such a patient, an extra three-month course of oral iron therapy should be prescribed.

Overt iron deficiency will usually respond satisfactorily to oral iron in the same dose as that advised for the immediate post-operative period.

However, occasional patients are intolerant of ferrous sulphate or gluconate or do not respond satisfactorily. In these circumstances they may benefit from chelated oral iron preparations (Hobbs, 1961), although in our experience it is usually necessary, and always expedient, to give such patients parenteral iron. Iron dextran (Imferon) is a satisfactory and the cheapest preparation for intramuscular administration, and one which in therapeutic doses has not been known to produce deleterious effects in man or in iron deficient experimental animals. Iron-citrate-sorbitol complex (Jectofer) may also be used and certain advantages have been claimed for this. The dosage of these injections is calculated from the degree of anaemia. Following the initial course of parenteral iron there is usually a satisfactory haematological response and, thereafter, an improvement in the tolerance of, and response to, oral iron.

The source of blood loss should be treated where possible. Stomal ulceration generally warrants operative treatment as, of course, does the presence of carcinoma. The treatment of oesophagitis with bleeding depends upon the aetiological factors present in the particular case but, as with piles or menorrhagia in patients having had gastrectomy, radical treatment is often indicated to prevent further blood loss.

VITAMIN B_{12} DEFICIENCY FOLLOWING GASTRIC OPERATIONS

Vitamin B_{12} Absorption

Recognition of the association of vitamin B_{12} deficiency with gastric malfunction ante-dates by many years the actual isolation of vitamin B_{12}. However, the classical hypothesis of Castle, namely that an extrinsic factor or vitamin B_{12} combined with an intrinsic factor secreted by the stomach to form a haematopoietic factor, has needed modification because vitamin B_{12} is active when given parenterally. Berk and colleagues (1948) have demonstrated that an intrinsic factor is necessary for the absorption of physiological amounts of vitamin B_{12}.

In man, intrinsic factor is a product of the body of the stomach. The upper two-thirds of the human stomach has been found to be most active from the haematopoietic point of view (Fox and Castle, 1942; Landboe-Christensen and Plum, 1948; Landboe-Christensen, Berk and Castle, 1952), and at autopsies on patients with pernicious anaemia the most severe mucosal atrophy has been found in the upper portion of the stomach, whereas the pyloric portion has shown either no abnormalities (Magnus and Ungley, 1938) or only partial changes (Meulengracht, 1939; Cox, 1943).

Although the intrinsic factor is secreted by the stomach there is considerable evidence that vitamin B_{12} is absorbed from the ileum (Booth and Mollin, 1957 and 1959; Cooke and colleagues, 1957; Cox and colleagues, 1958). Disease or excision of the lower ileum results in impaired B_{12} absorption.

Vitamin B_{12} absorption may also be impaired in the so-called blind loop syndrome. The malabsorption in this syndrome is associated with infection of small bowel diverticula or of peristaltically self-filling loops of bowel, usually produced by surgical operations. In this condition the impaired absorption of radioactive vitamin B_{12} can be corrected by parenteral or oral administration of the tetracyclines, chloromycetin or erythromycin, but not by antibiotics, such as neomycin, which are not absorbed from the alimentary tract (Halstead, Lewis and Gasster, 1956). This syndrome has been reported following Billroth II type gastrectomy and after gastro-enterostomy, the afferent loop acting as the blind loop.

Vitamin B_{12} Deficiency and Complete Gastrectomy

Although this book is concerned only with partial gastrectomy, observations following complete gastrectomy (usually performed for carcinoma) throw light on the aetiology of vitamin B_{12} deficiency.

The investigations of Castle and colleagues (1929 and 1953) indicate that pernicious or megaloblastic anaemia results from inadequate intrinsic factor production by the gastric mucosa. If pernicious anaemia is simply attributable to lack of intrinsic factor, one would expect that it would be an invariable sequel to complete gastrectomy.

Girdwood (1952) has shown that the normal daily requirement of vitamin B_{12} is approximately 1 μg, while the body stores are of the order of 1,000–2,000 μg. Consequently 3–6 years would be required to exhaust these stores. Table 9 shows the interval of time between gastrectomy and the development of megaloblastic anaemia as recorded by MacLean and Sundberg (1956), Welbourn, Nelson and Zacharias (1956) and Cox (1958). All but one patient took less than 7½ years to develop clinical evidence of vitamin B_{12} deficiency. Fellinger (1950) recorded megaloblastic anaemia in all eight patients who survived this operation for 5–8 years. Blake and Rechnitzer (1953) recorded an incidence of six out of ten patients 3–7 years after operation, and all four of Tomoda's series (1954), who had survived gastrectomy for four years, developed megaloblastic anaemia.

TABLE 9

The Time Interval Between Complete Gastrectomy and Presentation with Megaloblastic Anaemia

MacLean and Sundberg (1956) Years	*Welbourn, Nelson and Zacharias (1956)* Years	*Cox (1958)* Years
2½	4	2½
2½	4	2½
2½	5	4½
3	5	4½
3	6	5
3		7
3½		7
4		14
4		
4		
4		
5		
5½		
5½		
7½		

In the majority of patients after complete gastrectomy the absorption of radioactive vitamin B_{12} resembles that observed in pernicious anaemia (Callender, Turnbull and Wakisaka, 1954); in fact, its absorption may be even more severely impaired (Mollin, 1962). Absorption of B_{12} is corrected by the simultaneous administration of instrinsic factor. These observations and the gradual deterioration of serum B_{12} levels following complete gastrectomy complete this aetiological picture. In patients having had a complete gastrectomy there is no evidence of impaired folic acid absorption (Doig and

Girdwood, 1960), and the majority of such patients require only B_{12} therapy. However, supplementation with folic acid has been required on a number of occasions to convert an otherwise suboptimal haematological response to an entirely satisfactory one (MacDonald and colleagues, 1947; Conway and Conway, 1951; Arisjoshi, 1951; Beyers and colleagues, 1952; Larsen, 1952; Welbourn, 1956).

It is now generally accepted that all patients having had complete gastrectomy will eventually develop vitamin B_{12} deficiency and should be given parenteral vitamin B_{12} prophylactically. Nevertheless, it is surprising how frequently this precaution is omitted. Weight loss, malaise, dyspepsia, glossitis and mild neuropathy may persist for many months before the patient develops overt signs of a megaloblastic anaemia, and what may be a prolonged period of debility can easily be avoided by the prophylactic approach. One patient, who had a complete gastrectomy for hypertrophic gastritis, presented 18 months later with a foot drop and a subnormal serum B_{12} level. After three months' B_{12} therapy the patient's weight increased by 8 lb., his general well-being improved and his foot drop had cleared. His peripheral blood picture showed only a slight macrocytosis and the bone marrow showed a normal erythropoiesis. He later developed iron deficiency.

MEGALOBLASTIC ANAEMIA DUE TO VITAMIN B_{12} DEFICIENCY FOLLOWING PARTIAL GASTRECTOMY

Incidence

(Megaloblastic anaemia due to vitamin B_{12} deficiency is a rare complication of the post-partial-gastrectomy state) For many years, only sporadic cases have been reported, and published series have been small. Nieweg (1953) described six cases and Badenoch and colleagues (1955) described five; MacLean (1957) detected 9 out of 1,500, and Davidson (1959) 14 out of 500 partial gastrectomies. In our series of 100 post-gastrectomy patients investigated 5–6 years after operation, two had megaloblastic anaemia. In a series of patients with megaloblastic anaemia, amounting to over 800, one of the present authors (E. V. Cox) has observed only 15 occurring after partial gastrectomy. Even more rarely does this complication occur after simple gastro-enterostomy.

The Clinical Picture

(The clinical picture resembles pernicious anaemia.) The associated anorexia, nausea, vomiting and weight loss may suggest surgical complications, such as recurrence of ulcer, or neoplasm, but the presence of soreness of the tongue with an active or atrophic glossitis, peripheral paraesthesiae or even objective signs of subacute combined degeneration of the cord (absent, reduced or exaggerated tendon jerks, joint sense impairment, ataxia, loss of vibration sense and extensor plantar responses in varying combinations) help in the differential diagnosis. The diagnosis is confirmed by the presence of a macrocytic anaemia, megaloblastic erythropoiesis and a subnormal serum vitamin B_{12} level. A histamine fast achlorhydria, using the augmented histamine test of Kay (1953), is usually indicative of intrinsic factor deficiency, although achlorhydria may be wrongly diagnosed because of incorrect positioning of the gastric tube. Failure to absorb radioactive vitamin B_{12} which is corrected by the simultaneous oral administration of intrinsic factor, confirms the patient's failure to produce intrinsic factor (*Figure 42*). These patients may be differentiated from those with malabsorption due to a blind loop syndrome since, in the former, intrinsic factor corrects the absorption of the radioactive B_{12}, while in the latter B_{12} absorption is corrected by a course of tetracycline (see *Figure 45*).

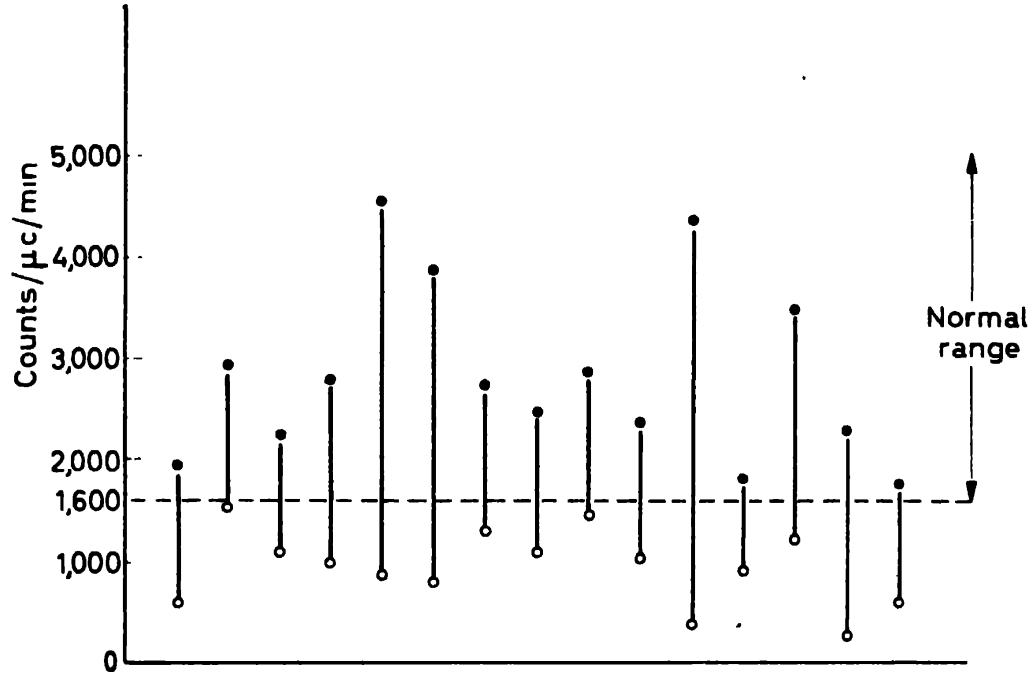

Figure 42. Surface hepatic counts per μc per min, one week after oral administration of ^{58}Co *labelled vitamin* B_{12} *(open circles), showing improvement of absorption when the test was repeated with the simultaneous oral administration of hog intrinsic factor (closed circles). All determinations performed on patients 5–6 years after partial gastrectomy for simple peptic ulceration*

Sub-clinical Deficiency of Vitamin B_{12}

Until recent years the term vitamin B_{12} deficiency has been virtually synonymous with megaloblastic anaemia. However, one index of B_{12} deficiency, namely a low serum B_{12} level as determined by microbiological assay with either *Lactobacillus leichmanni*, *Escherichia coli* or *Euglena gracilis*, has been observed in patients without megaloblastic anaemia. A report of a number of patients having had partial gastrectomy, who had iron deficiency and low serum B_{12} levels and yet no disorder in erythropoiesis, was presented by Cox and colleagues (1959).

(More recently, the incidence of low serum B_{12} levels in the post-gastrectomy state have been found to be far in excess of that of megaloblastic anaemia) Sewell (1961), Deller and Witts (1962) and Jones and colleagues (1962) found subnormal levels in 30 per cent, 14 per cent and 51 per cent of patients, respectively. The high incidence in our own series (Jones and colleagues, 1962) was probably the result of our selection of cases more than five years after operation (see *Figure 43*). Deller and Witts (1962) found a similar high incidence in their group 5–6 years after operation.

The Significance of a Low Serum B_{12} Level With Normal Erythropoiesis

Does a low serum vitamin B_{12} level, as detected by micro-biological assay, mean that the patient has a deficiency state? In patients where this is associated with a megaloblastic anaemia, and which can be observed to respond to vitamin B_{12}, the answer is obviously in the affirmative. However, in those patients with no decisive clinical findings the question cannot be answered with such certainty. It is possible, for example, that the serum B_{12} level does not always reflect the tissue content of this vitamin. The available evidence does support the conclusion that these patients are truly deficient. It may be summarized as follows:

(1) The tissue content, as indicated by the vitamin B_{12} level of bone marrow cells, is reduced when serum levels are low (Cox and colleagues, 1960).

(2) We have observed that some of these patients without megaloblastic changes have a mild macrocytosis, which disappears with vitamin B_{12} therapy (Williams, 1963).

(3) Other patients with low serum vitamin B_{12} levels but without anaemia have, after treatment with B_{12} alone, shown subjective symptomatic improvement and gain in weight (Williams, 1963).

(4) Although the bone marrow in many cases shows only a normoblastic erythropoiesis or, at the most, macronormoblastic

change, the peripheral white cell series often shows multi-segmented polymorphs, and the bone marrow giant forms of myelocytes and metamyelocytes; these findings, as stressed by Herbert (1959), are important in the early diagnosis of vitamin B_{12} deficiency.

(5) In similar patients we have shown an increased urinary excretion of methylmalonic acid, which is a metabolite found in excess only in B_{12} deficiency (Cox and White, 1962).

(6) A large proportion of these patients have impaired or low normal absorption of radioactive vitamin B_{12} [see *Figure 44* (Jones and colleagues, 1962)].

Thus, the available evidence strongly suggests that a low serum vitamin B_{12} level is usually indicative of a deficiency state, even in the absence of an established magaloblastic erythropoiesis.

Aetiology and Pathogenesis of Vitamin B_{12} Deficiency Following Partial Gastrectomy

The Character of the Lesion and the Nature of the Gastric Mucosa at the Time of the Operation—A reduction of intrinsic factor production, resulting from excision of a large part of the stomach, would at first seem to provide an explanation for the development of B_{12} deficiency. However, the absorption of radioactive vitamin B_{12} is unimpaired in the immediate post-gastrectomy period. Only a few square centimetres of gastric cuff is required to produce sufficient intrinsic factor for normal B_{12} absorption (Tanner, 1955; Lowenstein, 1958). Thus, the simple explanation of intrinsic factor deficiency, due solely to removal of part of the stomach, is obviously not correct. Nevertheless, by the time they develop megaloblastic anaemia, as the result of vitamin B_{12} deficiency, all patients show malabsorption of radioactive vitamin B_{12} which, in the majority of cases, can be corrected by the simultaneous administration of intrinsic factor and B_{12} (Badenoch and colleagues, 1955; Doig and Girdwood, 1960; and our own observations).

In some instances, changes are seen in the gastric mucosa at the time of operation which indicate that atrophic gastritis is already present. Nieweg (1953) reported two such patients who developed megaloblastic anaemia following partial gastrectomy and concluded that they were really suffering from pernicious anaemia. MacLean (1957) drew similar conclusions from studying, retrospectively, the gastric mucosa of the resected stomachs of nine patients in whom megaloblastic anaemia was diagnosed many years after gastrectomy. Rarely, megaloblastic anaemia may already be present at the time of operation, particularly when the operation is for carcinoma. Cox (1958) reported four patients who presented with simultaneous pernicious anaemia and gastric carcinoma; other similar examples have been recorded in the literature (Wilkinson, 1933).

We have also seeen two patients with pernicious anaemia who, on routine investigation, were found to have gastric polyposis. Geertruyden (1958), in a haematological study of 919 patients after partial gastrectomy, suggested that the development of megaloblastic anaemia was not related to the removal of part of the stomach but to the pre-operative state of the gastric mucosa. While admitting that megaloblastic anaemia was likely to occur when the operation was for gastric carcinoma or polyposis, he suggested that the incidence in patients operated on for simple ulcer was no higher than would be expected by chance.

Post-operative Gastritis—The incidence and aetiology of post-operative inflammatory and degenerative changes of the gastric mucosa have been discussed in Chapter 6. The conclusion which is reached is that after partial gastrectomy there is a gradual atrophy of the specific secretory cells of the gastric glands. Some patients, particularly those with gastric ulceration, are more likely to start with atrophic gastric glands, but even where the gastric mucosa is normal at the time of operation there is usually a gradual post-operative 'degeneration' of the gastric mucosa. The possible factors responsible for this atrophy are: (1) the state of the gastric mucosa at the time of operation; (2) gastritis as a result of reflux of duodenal juices through the stoma; (3) gastritis as a result of upper alimentary tract infection; and (4) chronic iron deficiency (see p. 130). Whatever the aetiology of the gastritis and mucosal atrophy, its presence is extremely important in the production of vitamin B_{12} malabsorption.

In five patients who developed a post-gastrectomy megaloblastic anaemia, Badenoch and colleagues (1955) found that biopsies of the gastric remnants showed gastric atrophy although, at the time of operation, all had normal gastric glands and four had free hydrochloric acid in their gastric secretions.

This glandular atrophy is probably not the result of an inherent pre-disposition, for in a recent paper it has been shown that patients who develop pernicious anaemia rarely have a history of peptic ulceration (Cox, 1962).

Low serum vitamin B_{12} levels and impaired radioactive vitamin B_{12} absorption are more common five years after gastrectomy for gastric than for duodenal ulceration (*Figures 43* and *44*).

It appears that one of the most important causative factors in gastric mucosal atrophy is duodenal reflux associated with a gastro-jejunal anastomosis and the most common operation performed for chronic duodenal ulceration is the Billroth II type with gastro-jejunostomy; one would therefore expect that, with the passage of time, vitamin B_{12} deficiency would become just as common when the operation was performed for duodenal as for gastric ulceration. This is indeed borne out by the observations of Doig and Girdwood (1960) who found that, of ten patients who developed megaloblastic anaemia after gastric operations, four had had their operation for gastric ulcer and six for duodenal ulcer.

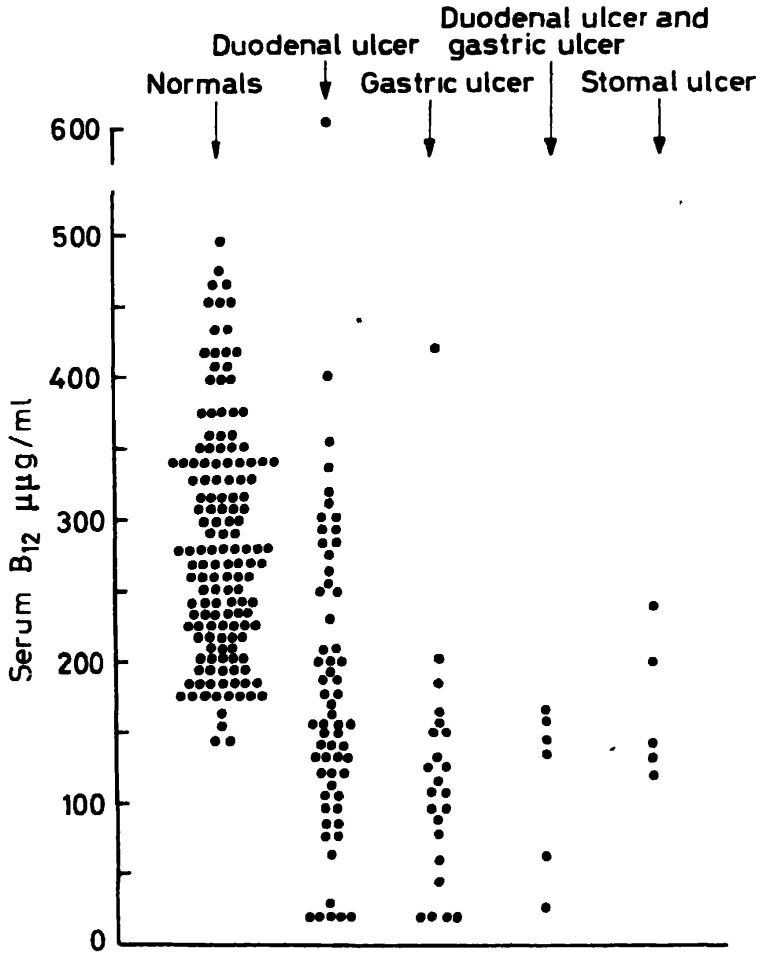

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Figure 43. Serum vitamin B_{12} levels (Lactobacillus leichmannii) *in normal patients compared with those in 100 patients 5–6 years after partial gastrectomy for duodenal and/or gastric ulceration and/or stomal ulceration* (Jones and colleagues, 1962)

In our series of fifteen patients with post-gastrectomy megaloblastic anaemia, seven had operations for gastric carcinoma, three for gastric ulceration, one for combined duodenal and gastric ulceration and four for duodenal ulceration. Three of the duodenal ulcer cases had been complicated by severe post-operative iron deficiency. The role of iron deficiency is discussed further on page 175

The Blind Loop Syndrome with B_{12} Deficiency—Occasionally, a blind loop syndrome develops following a Billroth II gastrectomy. As discussed in earlier chapters, the afferent loop occasionally drains

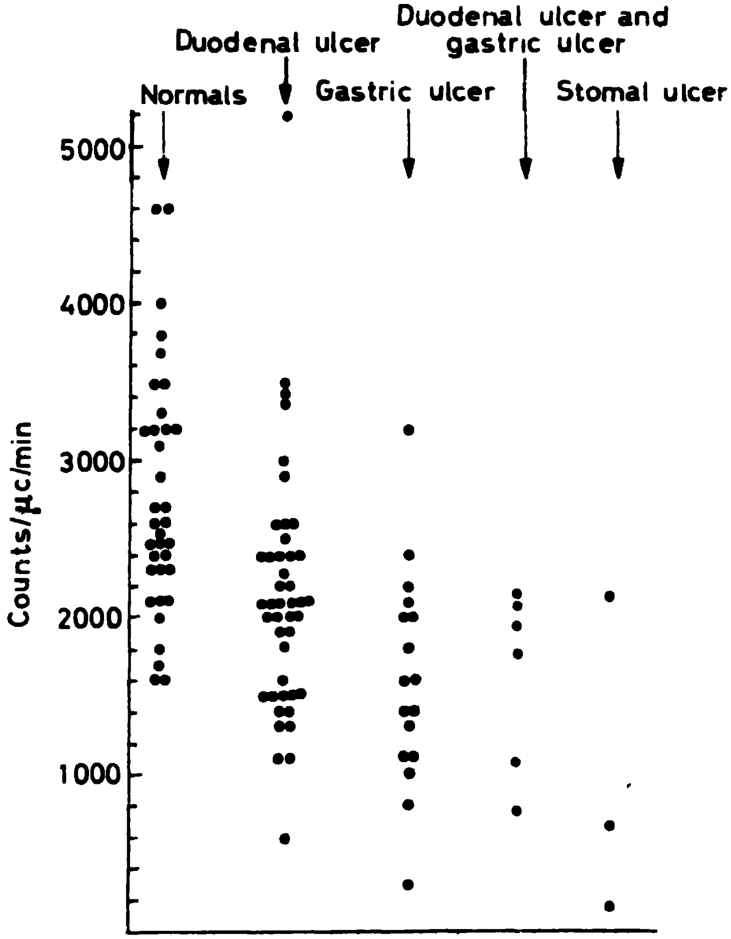

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Figure 44. Surface hepatic counts one week after the oral administration of ^{58}Co *labelled vitamin* B_{12} *in normal patients compared with patients 5-6 years after partial gastrectomy for duodenal, gastric or stomal ulceration (compare with Figure 43)*

imperfectly; B_{12} deficiency can develop in these circumstances despite the presence of intrinsic factor and adequate dietary vitamin B_{12}. The malabsorption is thought to be due to bacterial proliferation in the stagnating contents of a poorly emptying duodenal loop, with consequent interference with vitamin B_{12} absorption lower down. Examples of megaloblastic anaemia due to B_{12} deficiency as a result of a blind loop syndrome have been recorded by Naish and Capper (1953); Adams (1958); Kinsella and Hennessy (1960); Ragins and Oberhelman (1960); Hoffman and Spiro (1961); Goldstein, Wirts and Kramer (1961). Four cases were complicated by subacute combined degeneration of the cord (Adams, 1958; Naish and Capper, 1953; Butz, Hartman and Starzl, 1961; Goldstein, Wirts and Kramer, 1961). Hypoproteinaemia may also complicate the picture (Butz, Hartman and Starzl, 1961; Goldstein, Wirts and Kramer, 1961; Naish and Capper, 1953; Krikler and Schrire, 1958). As in other clinical examples of the blind loop syndrome, for example jejunal diverticulosis, or surgically produced blind loops, antibiotics improve or restore to normal the absorption of both vitamin B_{12} and fat (*Figure 45*). This fact is used for diagnostic as well as therapeutic purposes. However, when an established deficiency exists, parenteral B_{12} must be given without delay. Definitive therapy requires surgical correction, usually the conversion of a Billroth II to a Billroth I anastomosis. Good results were obtained in all six reported cases with complete or partial correction of the pre-existing absorption defects (Butz, Hartman and Starzl, 1961; Goldstein, Wirts and Kramer, 1961; Hoffman and Spiro, 1961;

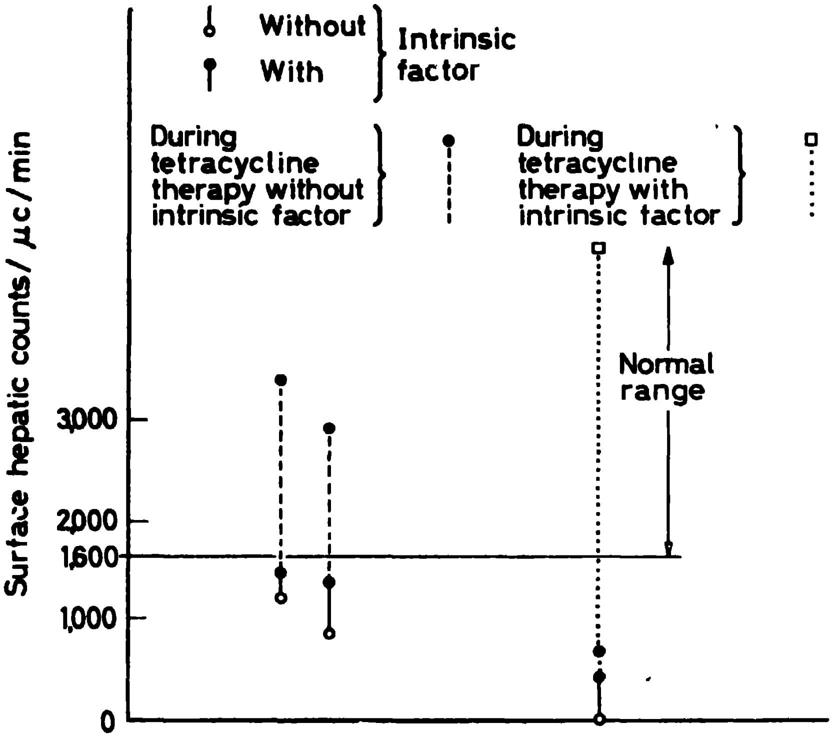

Figure 45. Left: ^{58}Co labelled vitamin B_{12} absorption in two patients with 'blind' afferent loop syndromes after partial gastrectomy; right: representation of the results in the case reported (see Table 10)

Naish and Capper, 1953; Ragins and Oberhelman, 1960). It is interesting to note that, of the 100 patients we studied 5–6 years after partial gastrectomy, two had evidence of a blind loop syndrome (Jones and colleagues, 1962). Occasionally, vitamin B_{12} deficiency after partial gastrectomy can be the result of both intrinsic factor deficiency and the blind loop syndrome. The following case report describes such a case.

A male, aged 68, had developed increasing pallor, weakness, dyspnoea with peripheral paraesthesiae and unsteadiness in walking. A Billroth II gastrectomy had been performed 13 years previously.

Clinically, there was evidence of severe anaemia, severe glossitis and a classical picture of subacute combined degeneration of the cord. His initial investigations were as follows: R.B.C. 1·19 million, Hb 5·1 g, P.C.V. 15 per cent, M.C.V. 120 μ^3, M.C.H.C. 34 per cent. The bone marrow examination revealed a grossly megaloblastic erythropoiesis. Serum vitamin B_{12} 40 $\mu\mu$/ml. Parenteral therapy with vitamin B_{12} produced a complete haematological remission and disappearance of his neurological signs. His average faecal fat excretion was 8·6 g/day. Histamine test meal showed no free HCl. Gastric biopsies revealed a complete gastric atrophy with only occasional dilated glands.

The radioactive vitamin B_{12} absorption tests are shown in Table 10. Only a combination of intrinsic factor and antibiotic restored normal absorption, indicating the presence of both an intrinsic factor deficiency and a blind loop syndrome.

TABLE 10

Radioactive Vitamin B_{12} Absorption in a Patient with a Billroth II Gastrectomy and Evidence of Deficiency of Intrinsic Factor and Blind Loop Syndrome (see also *Figure 45*).

Oral administration	*Liver counts per micro-curie per minute seven days later*
Radioactive vitamin B_{12} alone	0
Radioactive vitamin B_{12} + intrinsic factor	426
Radioactive vitamin B_{12} + tetracycline	611
Radioactive vitamin B_{12} + intrinsic factor and tetracycline	4,646

Role of Iron Deficiency—It should be remembered that many authors have suggested that chronic iron deficiency may be a contributory aetiological factor in pernicious anaemia, particularly in those patients in whom it has preceded pernicious anaemia (Campbell and Conybeare, 1922; Witts, 1930; Dameshek, 1931;

Miller and Dameshek, 1941; Mosbeck, 1953; Nelson and Weaver, 1956).

As we have seen, iron deficiency is a common complication of partial gastrectomy. Chronic iron deficiency, in patients who have had no operation and no upper gastro-intestinal disease, is often associated with a degree of gastric atrophy as severe as that seen in pernicious anaemia (Badenoch, Evans and Richards, 1957; Davidson and Markson, 1955; Joske, Finckh and Wood, 1955). In animals, the secretion of intrinsic factor may also be impaired by severe iron deficiency (Hartfall and Witts, 1933), an observation which has been confirmed in man using radioactive vitamin B_{12} (Badenoch, Evans and Richards, 1957), and in rats (Taylor and Witts, 1958).

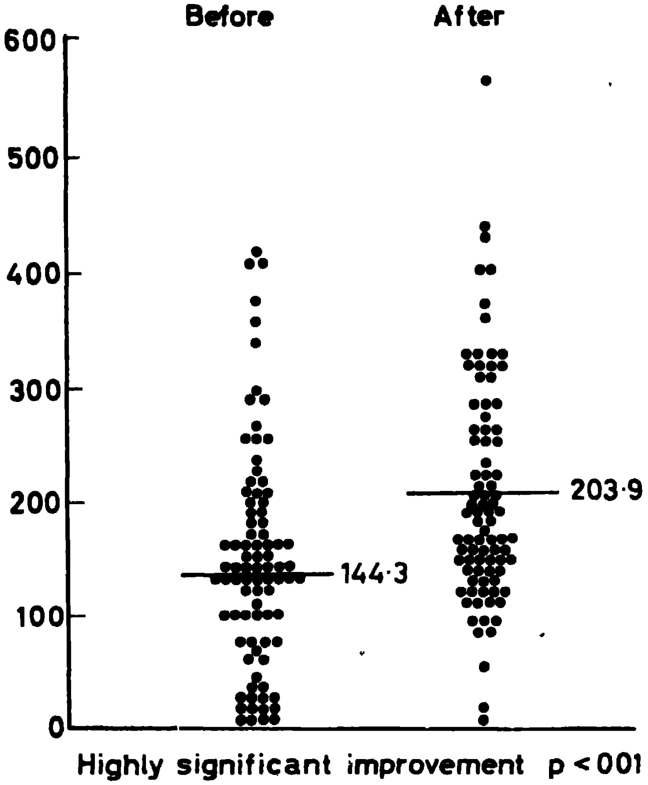

Figure 46. Left: Serum vitamin B_{12} levels (Lactobacillus leichmannii) *in patients 5–6 years after partial gastrectomy (see Figure 43), compared with the levels in the same group of patients (right) after a three-month course of oral ferrous gluconate*

In 1959 we reported a group of patients with iron deficiency and subnormal serum vitamin B_{12} levels. The serum vitamin B_{12} levels in these patients, which included five with partial gastrectomy, gradually returned to normal with iron therapy. It was then suggested that these patients had an actual deficiency of vitamin B_{12}, which was restored when the absorption of this vitamin was corrected by iron therapy (Cox and colleagues, 1959). In a larger series of patients 5–6 years after partial gastrectomy, we found low serum vitamin B_{12} levels in all with iron deficiency anaemia, and in 75 per cent of those without anaemia but with evidence of iron deficiency as shown by a raised serum total iron binding capacity, low serum iron or microcytosis (Jones and colleagues, 1962).

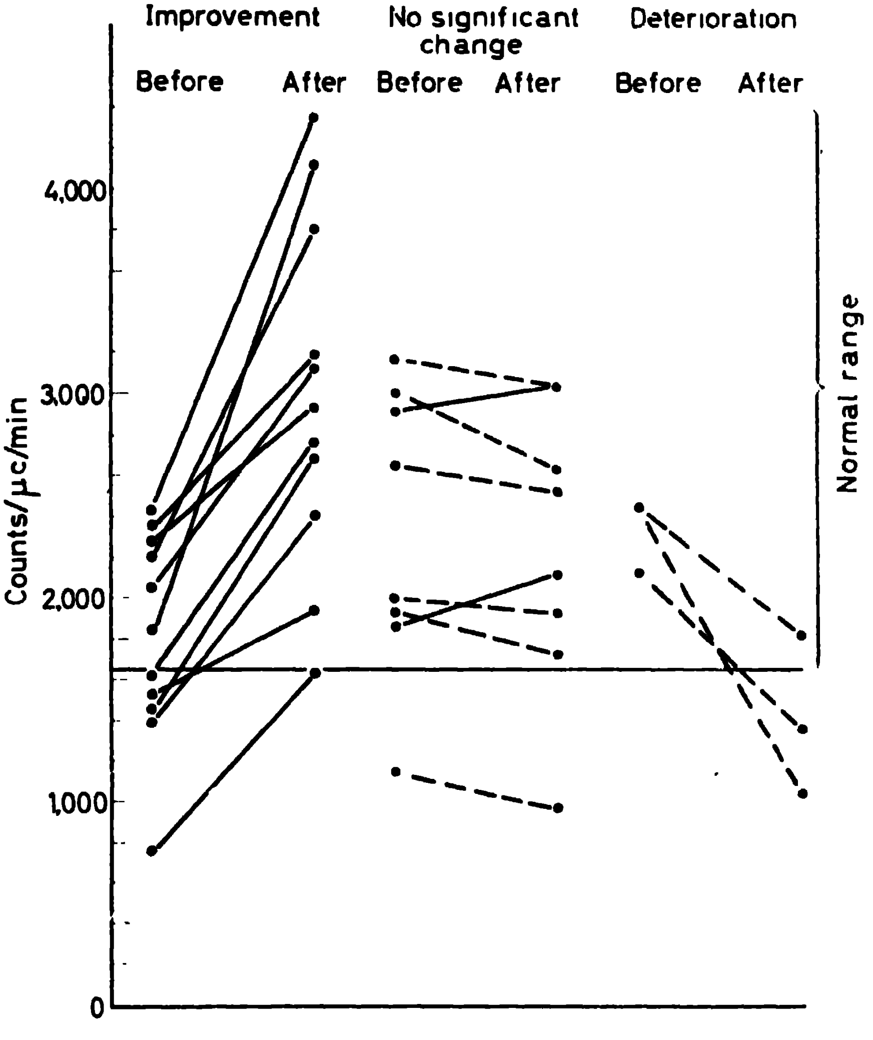

Figure 47. Surface hepatic counts one week after the oral administration of ^{58}Co *labelled vitamin* B_{12} *in post-gastrectomy patients before and after a three-month course of oral ferrous gluconate*

In 57 per cent of these iron-deficient patients the absorption of radioactive vitamin B_{12} was subnormal and was improved by the administration of intrinsic factor. The degree of impairment of vitamin B_{12} absorption in most cases was not as severe as that which occurs in pernicious anaemia. Iron therapy not only improved the serum vitamin B_{12} level in the group as a whole (*Figure 46*) but also improved the absorption of radioactive vitamin B_{12} in 12 out of 23 patients (*Figure 47*) (Williams, Jones and Cox, 1962). These observations support the hypothesis that iron deficiency can adversely affect the gastric mucosa so that intrinsic factor secretion is impaired. This effect of chronic iron deficiency on the gastric lining is probably greater in patients with abnormal stomachs, which accounts for the high incidence of its occurrence in patients with partial gastrectomy.

In many of these patients, the effect of iron deficiency on gastric function is reversible, in that intrinsic factor production appears to be improved by appropriate iron treatment. However, biopsy of the gastric remnant in two patients showed no apparent change after a three-month course of iron therapy. Longer studies may be required to demonstrate any histological improvement. In one patient with subnormal vitamin B_{12} absorption, iron therapy for three months (Table 11) produced no improvement, and in three others vitamin B_{12} absorption deteriorated. It seems probable that the patients in which B_{12} absorption did not improve were examples of gastric mucosal atrophy due to other causes, or that they had progressed to an irreversible state prior to the administration of iron. In the latter instance, if there is a severe iron deficiency, the correction of this increases erythropoiesis and possibly the demand for vitamin B_{12}, and because of the irreversibly impaired absorption of vitamin B_{12} the effects of B_{12} deficiency is accentuated and megaloblastic anaemia is precipitated. The following case report illustrates this.

A male, now aged 60, had a gastro-enterostomy for duodenal ulceration in 1930 and a Billroth II gastrectomy for duodenal and stomal ulceration in 1947. He was treated in 1953 for bilious vomiting and diarrhoea. The latter was found to be associated with steatorrhoea and this was improved by the administration of pancreatin with food. On admission in 1959 he complained of progressive weakness, lethargy and of more recent dvspnoea, pallor and angina pectoris. Clinically, he was extremely pale and dyspnoeic on the slightest exertion. The tongue was smooth and atrophic. There were no other physical abnormalities. Red blood cells 3·20 million; haemoglobin 4·8 g; serum iron 10 μg/100 ml; serum B_{12} 12 $\mu\mu$g/ml. Four examinations for occult blood were negative and no bleeding site was demonstrated radiologically. Oral iron therapy produced a striking clinical improvement and 11 weeks later his blood picture was as follows: red blood cells 4·4 million; haemoglobin 13·1 g; P.C.V. 45; M.C.V. 102 μ^3; M.C.H.C. 29·5 per cent; his serum vitamin B_{12} had risen to 180 $\mu\mu$g/ml. Over the next six months his condition gradually deteriorated despite continued iron therapy, and at the end

TABLE 11

A Male Patient Aged 60 who, Ten Years Previously, had a Polya Gastrectomy for Duodenal Ulceration. He Presented with Iron Deficiency Anaemia and Subsequently Developed Vitamin B_{12} Responsive Megaloblastic Anaemia

	R.B.C. million	*Hb* g per cent	*P.C.V.* per cent	*M.C.V.* μ^3	*M.C.H.C.* per cent	*Weight* lb.	*Serum* B_{12} $\mu\mu$g/ml	*Remarks*
On presentation	3·2	4·8	—	—	—	112	>25	Predominantly Fe deficient. Marrow normoblastic
After 3/12 iron therapy	4·4	13·1	45	102	29·5	117	180	Becoming macrocytic. Normal B_{12}
After 9/12 iron therapy	3·27	11·0	37·5	114	30·5	115	80	Marrow frankly megaloblastic
After 3/12 B_{12} therapy	4·75	14·0	45	90	32·0	124	—	Normal

of this time his blood values were as follows: red blood cells 3·27 million; haemoglobin 11·0 g; P.C.V. 37·5; M.C.V. 114 μ^3; M.C.H.C. 30·5 per cent; serum B_{12} 80 $\mu\mu$g/ml. Vitamin B_{12} absorption was within the range seen in pernicious anaemia, but the test was not repeated with the addition of intrinsic factor or antibiotics. His bone marrow now showed megaloblasts for the first time. Vitamin B_{12} therapy restored normal blood values. His general well-being again improved and during the following three months he put on 9 lb. in weight (see also Table 11).

Low Serum Vitamin B_{12} Levels with Normal Vitamin B_{12} Absorption

Malabsorption of vitamin B_{12} does not completely explain the incidence of low serum vitamin B_{12} levels following partial gastrectomy. We observed that 43 per cent of patients with low serum vitamin B_{12} following this operation had normal absorption (Jones and colleagues, 1962). Dietary deficiency may be an explanation, although dietary histories did not suggest that this was an important factor. The majority of these patients had an associated disturbance of iron metabolism and it seems possible that iron deficiency or chronic blood loss may increase the demand for vitamin B_{12} in excess of the limited ability of the ileum to absorb this vitamin. Certainly, iron therapy restores the serum B_{12} level in some of these patients (Cox and colleagues, 1962a). If this argument is taken one step further, the possibility exists that this type of vitamin B_{12} deficiency in itself may adversely affect gastric function, since in severe deficiency, as occurs in pernicious anaemia in relapse, the appearance of the gastric mucosal cells is grossly abnormal (Graham and Reault, 1954).

The Detection and Investigation of B_{12} Deficiency Following Gastric Operation

All investigations can easily be carried out on out-patients. Venous blood is taken for the determination of the standard haematological indices (P.C.V., M.C.V. and M.C.H.C.), serum vitamin B_{12}, serum iron and total iron binding capacity. The serum B_{12} is estimated microbiologically, and we use the organism *Lactobacillus leichmanni* (Meynell and colleagues, 1957). The procedure has been modified by the addition of cyanide to the extraction medium (Spray, 1955). An excellent assessment of this method has recently been made by Matthews (1962), in whose articles complete details are available. The availability of commercially prepared assay media make this a suitable method for clinical laboratories.

Where the serum vitamin B_{12} level is subnormal, the investigation is completed by studying the absorption of radioactive B_{12}. Where facilities are available this can be performed simply by the method of surface hepatic counts (Glass and colleagues, 1954; Fone and colleagues, 1961). After an initial count for 5 min, using a directional scintillation counter placed over the area of the liver (we use the junction of the eighth rib and the right anterior axillary line), the patient is given $\frac{1}{2}$ μc of cobalt 58—labelled B_{12} (1 μg/μc). A week later a second count is made over the liver. An increase in the second count over the initial count above 1,600 μc/min indicates normal absorption. A count below 750 is in the range associated with pernicious anaemia and complete gastrectomy.

Where low, counts are repeated one week later because unexplained delays occasionally occur in the hepatic up-take. Patients with subnormal counts are then tested again with the simultaneous administration of radioactive B_{12} and commercially prepared intrinsic factor. If the hepatic counts then rise to within the normal range the B_{12} malabsorption is due to deficiency of intrinsic factor. To patients who still have abnormal absorption, tetracycline 250 mg/day is administered for seven days, an don the fourth day a further test dose of radioactive B_{12} is administered. Normal B_{12} absorption in these circumstances indicates the presence of an infected blind loop but not inadequacy of intrinsic factor.

We have already recorded (p. 178) the case of one patient who required antibiotics and intrinsic factor to produce normal B_{12} up-take, indicating both an afferent loop 'blind loop syndrome' and intrinsic factor deficiency. The investigation of B_{12} absorption by the method of surface counting requires the patient to attend at weekly intervals for up to four weeks but each attendance is only for 5–10 min, and no urine or faecal collections are required. On any of these visits a gastric biopsy can be obtained using a Wood's tube or a modified Crosby capsule (see Chapter 6). The gastric biopsy can be performed in a few minutes and provides more information, from a haematological point of view, than the more uncomfortable and lengthy procedure of an augmented histamine response.

The Treatment of B_{12} Deficiency

Patients with defective radioactive vitamin B_{12} absorption, similar to that found in pernicious anaemia, require parenteral B_{12} therapy for life, and the association with gastric atrophy confirms this requirement. This includes not only the majority of patients with a megaloblastic anaemia, but also a number of patients who have less obvious signs of vitamin B_{12} deficiency. The response of the latter to therapy is usually dramatic and as satisfactory as in pernicious anaemia. Recent observations have shown that hydroxocobalamin [Neocytamen (Glaxo) in the United Kingdom, or Redisol (Merck, Sharp and Dohme) in the U.S.A.] gives more prolonged effect than cyanocobalamin and, after an initial saturation with 1,000 μg intramuscularly every week for four weeks, satisfactory maintenance can then be carried out with 250 μg monthly or 1,000 μg bimonthly (Cox, Meynell and Cooke, 1962).

Patients with the blind loop syndrome will also require parenteral vitamin B_{12} therapy, although following the conversion from Billroth II to Billroth I type anastomosis, this may no longer be necessary.

In those patients with vitamin B_{12} absorption below the normal range and yet above that of pernicious anaemia, it is difficult to know whether or not to give regular injections of vitamin B_{12}. When there is an associated disturbance in iron metabolism (hypochromia, microcytosis, low serum iron or raised serum iron binding capacity), the serum vitamin B_{12} and vitamin B_{12} absorption should be re-assessed after 3–6 months therapy with oral iron. In our experience this will frequently restore normal vitamin B_{12} absorption and a normal serum B_{12} level (Table 11). Patients showing no improvement or a deterioration in vitamin B_{12} absorption, will require parenteral vitamin B_{12}.

If labelled vitamin B_{12} absorption is within the normal range, iron therapy, when indicated, will usually restore low serum vitamin B_{12} levels to normal. In those patients not responding to this therapy—as, also, in the occasional patient with no evidence of iron deficiency—it may be justifiable to give oral vitamin B_{12} [Cytacon (Glaxo)], 50 μg twice a day. We have observed two patients who maintained normal serum vitamin B_{12} levels in this way, but in neither was there any symptomatic or objective improvement.

Folic Acid Deficiency

Macrocytic anaemia, associated with a megaloblastic erythropoiesis, glossitis, weight loss, diarrhoea, an absence of neurological symptoms or signs and no evidence of deficiency of vitamin B_{12}, is usually accepted as indicating the features of deficiency of folic acid or related pteroylglutamate compounds. Such an assumption is based on the clinical and haematological remission induced by the administration of a synthetic compound, folic acid.

(The occurrence of this syndrome in patients following partial gastrectomy is extremely rare and Deller and Witts (1962) observed it in only 3 out of 241 patients.) We have recently observed two cases.

The first patient, a male, had a Billroth II partial gastrectomy for duodenal ulceration in 1955, at the age of 55. In 1960 he presented with a severe iron deficiency (R.B.C. 2·92 million/ml; haemoglobin 5·2 g per cent; W.B.C. 7,200/ml; P.C.V. 23 per cent; M.C.V. 79 μ^3; M.C.H.C. 22·5 per cent). His serum iron was 11 μg/100 ml. Intramuscular iron produced an initial response, but the blood count 80 days later had become static at R.B.C. 3·46 million/ml; haemoglobin 9·8 g per cent; P.C.V. 37 per cent; M.C.V. 106 μ^3; M.C.H.C. 26·5 per cent. The serum vitamin B_{12} level and radioactive vitamin B_{12} absorption were normal. The bone marrow examination revealed a megaloblastic erythropoiesis. There was no steatorrhoea. Folic acid, 5 mg three times a day, produced a reticulocytosis and later a full haematological remission.

The second patient, a male aged 54, had undergone a Billroth II partial gastrectomy seven years previously for duodenal ulceration. On presentation he was confused, anaemic and had a severe glossitis. Investigations were as follows: R.B.C. 2·61 million/ml; haemoglobin 10·1 g per cent; P.C.V. 32 per cent; M.C.V. 123 μ^3; M.C.H.C. 31·5 per cent. Serum vitamin B_{12} was normal (235 $\mu\mu$g/ml) and vitamin B_{12} absorption was also normal. Serum folic acid activity was less than 1·0 mμg/ml (lower limit of normal 3·1 mμg/ml) assayed with *Lactobacillus casei*. In view of the patient's confused state he was given massive injections of vitamin B_{12} before the laboratory data were available. He responded to this therapy, but this does not negate the conclusion that he had a folic acid deficiency because, in some instances, large doses of vitamin B_{12} will produce a haematological response in this condition (Zalusky, Herbert and Castle, 1962). This patient later required iron therapy to achieve a haematological remission.

It is of interest that both these patients had had Billroth II gastrectomies, especially since there is evidence to show that the absorption of folic acid takes place in the duodenum and jejunum (Cox and colleagues, 1958). Following partial gastrectomy, however, there is no evidence of malabsorption of folic acid as judged by the urinary excretion following first, the intramuscular injection of 5 mg folic acid and then, 48 hours later, a similar dose administered orally (Girdwood, 1956; Cox and colleagues, 1958). Patients with folic acid deficiency due to the malabsorption syndromes react rather paradoxically in that they frequently absorb folic acid better than patients with the same underlying condition and without anaemia (Anderson and colleagues, 1960; Cox, Meynell and Cooke, 1961).

Both our patients had iron deficiency; out of patients with partial gastrectomies three had sub-normal folic acid activity in their sera, and each of those patients had chronic iron deficiency. It is possible that iron deficiency may, in some way, initiate the development of folic acid depletion, and the complication may be due to this, rather than to the associated partial gastrectomy.)

Scurvy and Partial Gastrectomy

Scurvy in the partial gastrectomized patient is a great rarity. We have recently described a case (Cox and colleagues, 1962b).

> This patient had had a partial gastrectomy 20 years previously. In order to avoid dyspepsia he had taken a diet consisting solely of fish, chicken occasionally, bread, butter and tea for four years. When he presented he had the classical features of scurvy, a bright purpuric rash over the legs, bruising and induration down the back of the legs, evidence of a haemarthrosis in the right knee and ankle, a foetid gingivitis and follicular hyperkeratosis over the forearms and buttocks. Investigations were as follows: R.B.C. 2·13 million/ml; haemoglobin 5·8 g per cent; P.C.V. 20 per cent; M.C.V. 94 μ^3; M.C.H.C. 29 per cent; and serum B_{12} level 210 $\mu\mu$g/ml. While continuing on the same diet he was cured by the addition of ascorbic acid, although he later required oral iron therapy.

Though this record is probably unique, it stresses the lengths to which patients will alter their diet to avoid symptoms. Less severe changes will naturally colour other deficiency conditions that occur in partially gastrectomized patients.

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9

DISTURBANCES OF BONE METABOLISM AFTER PARTIAL GASTRECTOMY

('POST-GASTRECTOMY BONE DISEASE')

C. Tasman Jones, John A. Williams and Gordon Nicholson

After investigating the calcium and phosphorus balances in a number of post-gastrectomy patients, Nicolaysen and Ragard (1955) stated 'The practical implication is clear . . . such negative calcium balances as here reported cannot continue for years without serious consequences'.

Our own observations, in addition to those of Clark, Crookes and Mitchell (1962) of Aberdeen, confirm the suggestion of Candian, Della Costa and Furlan (1959) that minor bone changes are common after partial gastrectomy. However, severe pathological bone disease is only rarely reported. Most of these reports are summarized in Table 12 and discussed on p. 202.

The normal development of bone and the maintenance of normal bone structure require an adequate supply of calcium, phosphorus, amino acids, calories and vitamins from the diet. The effects of upper gastro-intestinal operations on the absorption and metabolism of proteins is described in Chapter 10. The present chapter deals with the effects of alteration of calcium, phosphorus and vitamin D metabolism. For a full account of normal bone metabolism the reader is referred to the monographs on the subject by Malm (1958) and Fourman (1960), to the symposium edited by Rodahl, Nicholson and Brown (1960) and to the writings of Nicolaysen, Eeg-Larsen and Malm (1953) and Nordin (1960).

NORMAL METABOLISM

Calcium

The main sources of calcium in the diet are milk and cheese. One pint (540 ml) of milk contains approximately 700 mg of calcium. In Great Britain calcium is added to some bread, a practice which began with the war-time 'National Loaf' (McCance, 1946). The adult daily requirement of calcium is estimated as 10 mg/kg body-weight, a total of 600–800 mg (Steggerder and Mitchell, 1946).

Many people, however, take very much less than this in their diet with no apparent ill-effects (Hegsted, Moscoso and Collazos, 1952; Pollack, 1956).

Intake—A normal adult diet in Great Britain contains about 1,200 mg of calcium (National Food Survey, 1953), of which only about 200 mg are absorbed. With a low calcium diet, it is possible, however, for some individuals to achieve, by adaptation, almost 100 per cent absorption, provided that there is an adequate supply of vitamin D (Liu, 1928; Nicolaysen and Eeg-Larsen, 1956) but Malm (1958) has shown that not all are able to do so. In some parts of the world the dietary intake of calcium is as little as 200 mg/day (Pollack, 1956).

Absorption—An active transport mechanism for calcium exists in the small bowel. Absorption is greatest in the most proximal segments of the small intestine and decreases progressively in the more distal segments (Schachter, Dowdle and Schenker, 1960). There appears to be facultative control of calcium absorption to meet individual needs, absorption increasing with growth and pregnancy, as well as during periods of calcium depletion, while decreasing with age and a reduced calcium demand (Malm, Nicolaysen and Skjelkvale, 1955). Schachter and Rosen (1959) suggested that the parathyroid hormone may play a part in regulating calcium absorption, but Fourman (1960) thought that there was little evidence of any endocrine control.

Vitamin D is essential for the normal absorption of calcium, but in healthy adults on an already normal diet the daily administration of 2,000 I.U. of vitamin D does not increase the calcium absorption significantly (Jeans and Stearns, 1938; McCance and Widdowson, 1944).

The absorption of calcium may be enhanced by: acidity of the intestinal tract (Stewart and Percival, 1928; Kay, 1932; Schmidt and Greenberg, 1935; Bills, 1935); calcium depletion (Stearns and Moore, 1931); a high protein diet (McCance, Widdowson and Lehmann, 1942); or extra calcium needs, such as growth, pregnancy and lactation (Liu and colleagues, 1941).

Although the evidence for this is not conclusive, the absorption of calcium is said to be impaired by the presence in the gut of substances which form insoluble calcium salts. These are:

(1) Dietary phytic acid. Phytic acid occurs in the outer coats of the grains of many cereals, particularly wheat. It was for this reason that the war-time 'National Loaf' had additional calcium added (McCance, 1946).

(2) Fatty acids which form insoluble calcium soaps. However, a high fat diet does not, in itself, interfere with calcium absorption (Aub, Tibbetts and McLean, 1937).

(3) Excess of dietary phosphorus. This hypothesis, suggested by animal experiments, has not been supported by observations in man (Malm, 1958; Irving, 1957).

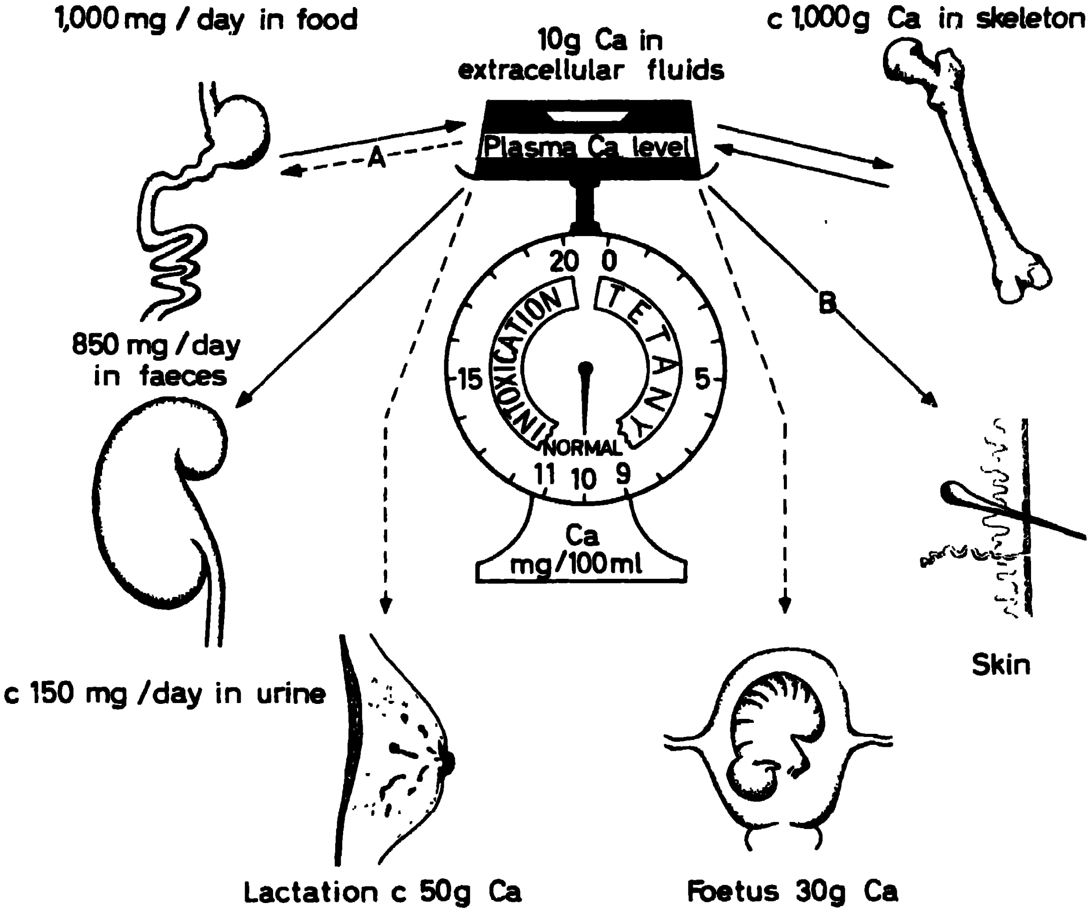

Figure 48. Calcium metabolism and transport. There is as yet no accurate assessment of the amount of calcium re-excreted in the gut (A) or lost in sweat (B) (after Dent, 1956)

Losses—Calcium is excreted in the urine and faeces and is also lost during pregnancy and lactation; as much as 100 mg/day may be lost in sweat (Malm, 1958). The intestinal secretion of calcium probably occurs primarily in the small bowel.

Much of the secreted calcium is undoubtedly re-absorbed, so that there is a calcium cycle, from which the net loss has been estimated as being approximately 70 mg/day. Excessive losses of calcium in the faeces occur in steatorrhoea (Meroney and colleagues, 1959), but this is almost certainly not due to vitamin D deficiency resulting from impaired fat absorption, because these calcium losses can occur in patients ingesting more than adequate amounts of vitamin D, in whom at least 80 per cent of the fat is absorbed. Furthermore, Badenoch and Fourman (1954) found that in patients with steatorrhoea the provision of additional dietary vitamin D, while improving calcium absorption, did not restore it to normal. It has not even been proved that vitamin D deficiency actually occurs in steatorrhoea since, even when patients with this abnormality are given a large dose of vitamin D, none can be recovered in the faeces (Fourman, 1960). Other factors leading to excessive faecal losses in steatorrhoea may be the formation of insoluble calcium salts of fatty acids or excess calcium secretion from the bowel (Fink and Laszlo, 1957).

The urinary excretion of calcium is normally never more than 400 mg, and is usually less than 200 mg. Diffusible calcium is filtered by the glomeruli but more than 99 per cent is re-absorbed in the tubules. Urinary calcium excretion may fall to 5–50 mg/day in vitamin D deficiency, hypoparathyroidism and chronic renal failure.

Phosphorus

Deficiency of phosphorus never arises as a nutritional problem because the element is found in most foods, particularly in association with proteins. About two-thirds of the dietary intake is normally absorbed. Phosphorus excretion occurs in the kidneys both by filtration and by tubular secretion (Nicholson and Shepherd, 1959). The diagrammatic representation by Dent (1956) is shown in *Figure 49.*

Vitamin D

Vitamin D_2 produced by the ultra-violet irradiation of ergosterol is called ergocalciferol or, more commonly, calciferol. The vitamin that is produced naturally by animals, vitamin D_2, is formed by the irradiation of 7-dehydrocholesterol and is called cholecalciferol. The anti-rachitic activity of these two vitamins in man is approximately equal. There is no such substance as vitamin D_1.

The daily adult requirement of vitamin D is probably less than 100 units, but that of children and pregnant or lactating women is much greater (400–800 units). In many parts of the world vitamin D is produced in the individual's skin by the action of ultra-violet rays from the sun. In this country and in many temperate and industrialized countries the major sources of vitamin D are fortified foods, such as dried milk, infant cereals and margarine.

According to Fourman (1960), very little is known of the fate of calciferol in the body. Since it is a sterol it is presumably absorbed in a similar manner to cholesterol and is probably more difficult to absorb than most dietary fats. Stores of vitamin D occur in the liver. Vitamin D is essential for the intestinal absorption of calcium and for this purpose small quantities only are required. Larger quantities are required to restore rachitic bones to normal. It is concerned with maintaining the normal structure of bone and helps to govern the equilibrium between blood and bone calcium (McLean, 1941).

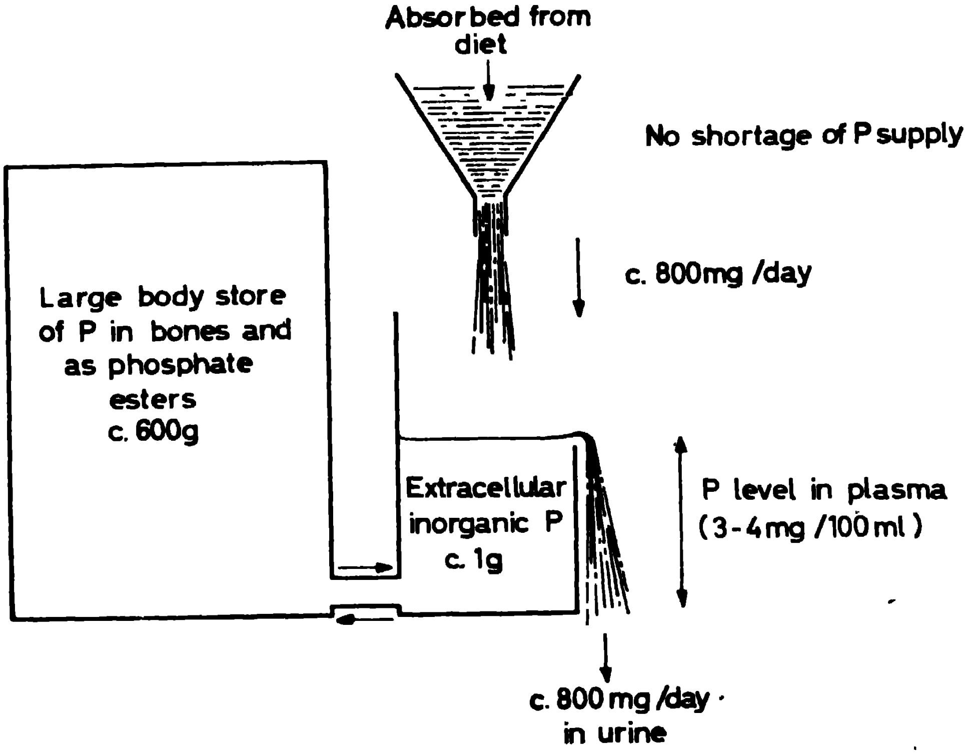
Absorbed from diet
No shortage of P supply
Large body store of P in bones and as phosphate esters c. 600g
c. 800mg /day
Extracellular inorganic P c. 1g
P level in plasma (3-4mg /100ml)
c. 800 mg /day in urine

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Figure 49. Phosphorus metabolism and transport (Dent, 1956)

Vitamin D also has an effect on the kidney, where its action is to lower the renal threshold and so increase excretion of calcium and phosphorus.

THE POSSIBLE EFFECTS OF UPPER GASTRO-INTESTINAL SURGERY

The physiological effects of gastric operations are discussed in Chapter 11. Calcium deficiency may arise as a result of:

(1) Reduced dietary intake after operation. Apart from the reduction of appetite and disinclination to eat large meals, which commonly follows partial gastrectomy (see Chapter 10), there

is often a specific reduction in the intake of milk (see p. 145). Apart from Great Britain, where calcium carbonate is added to bread flour, milk is the principal dietary source of calcium in most countries.

(2) Reduced absorption, which may be due to:
   (i) hypochlorhydria or achlorhydria;
   (ii) loss of the 'hopper' effect of the antrum;
   (iii) duodenal by-pass;
   (iv) the incomplete absorption of fats.

(3) Abnormal calcium losses from the alimentary tract, when there is alteration of jejunal mucosal structure or function.

There is little precise information about the effects of partial gastrectomy on vitamin D metabolism. Dietary idiosyncrasies after operation may lead to patients avoiding those foods which are the richest sources of vitamin D, such as margarine (which is fortified), egg yolk, milk and butter.

METABOLIC BONE DISEASE

Before discussing the observed effects of gastric operations on bone metabolism in animals and in man, it is necessary to consider the definition and aetiology of the expected bone disorders.

Osteomalacia

The adult counterpart of rickets, osteomalacia is the result of deficiency of vitamin D in patients who have ceased growing. It was first distinguished from other forms of bone softening by its characteristic histological picture by Pommer (1885) and was later recognized as having the same aetiology as rickets by Looser (1908). It is a condition where there is a normal amount of bone osteoid which is incompletely calcified. In osteomalacia symptoms may be absent for some time and when they occur they often begin as vague muscle aches and weaknesses. Fourman (1960) states that 'patients with osteomalacia complaining of inconstant pains in a variety of places have often been dismissed as neurotic'.

The pathological picture of the bones is one of excess osteoid tissue which on bone biopsy can be measured on the trabeculae. Osteoid seams of greater than 12μ in thickness seen on undecalcified sections are said to be diagnostic of osteomalacia (Ball, 1960), although in our experience some wide seams are found in normal bone biopsies. There is occasionally excessive osteoclastic activity, indicating secondary hyperparathyroidism.

Osteomalacia is characterized by a failure of absorption of calcium and a urinary calcium output below 80 mg/day (Anderson, 1961). There is no failure of phosphorus absorption and its urinary excretion is high. The serum calcium level is usually low; nevertheless, it is sometimes normal, kept so by the secondary hyperparathyroidism which removes calcium from the bones. The hyperparathyroid activity leads to excess phosphorus losses from the kidneys and often, in consequence, to a low serum phosphorus level (Nicolaysen and Eeg-Larsen, 1956). The serum alkaline phosphatase is usually slightly elevated, but may be normal.

The characteristic radiological finding in osteomalacia is the pseudo-fracture or 'Umbauzonen' of Looser (1920) (see *Figure 58*). These are usually symmetrical and are most often seen in the necks of the femora, humeri and in the pubic rami, ribs and scapulae. They are not true fractures and are not tender on pressure or on 'springing' the bone. They represent failure of re-calcification of areas of stress where bone remoulding has occurred (Kind, 1947). Generalized homogenous loss of bone density may also occur.

Osteoporosis (*Figure 50*)

The view of Albright and Reifenstein (1941) was that osteoporosis was a defect of bone matrix and was not due to any disorder of calcium metabolism. They postulated that bone matrix formation was regulated by hormones closely related to the gonadal hormones, and that osteoporosis was associated with a negative nitrogen balance. This classical view has recently been challenged by Nordin (1960 and 1961), who defined osteoporosis as a reduction in the amount of bone without any change in its chemical composition. Nordin suggested that primary osteoporosis could be due to a long-continued, negative calcium balance.

He calculated that over 8 per cent of the normal population of this country were taking insufficient calcium in their diet. Adaptation to a low calcium intake can occur in many people, but not in all (Malm, 1958); it is these people with an apparent obligatory high urinary calcium excretion who are most likely to show signs of osteoporosis if they have a deficient intake, impaired absorption or increased intestinal losses. Nordin's view was supported by the work of Harrison, Fraser and Mullan (1961). However, the data on which these hypotheses are based is, so far, insufficient to justify their general acceptance.

Osteoporosis and osteomalacia frequently co-exist, particularly in conditions such as gluten enteropathy and sprue [(Atkinson, Nordin and Sherlock, 1956; Lichtwitz and colleagues, 1961) (see *Figure 51*)].

Urist (1960) described osteoporosis as loss of bone mass with gative calcium, phosphorus and nitrogen balance though normal

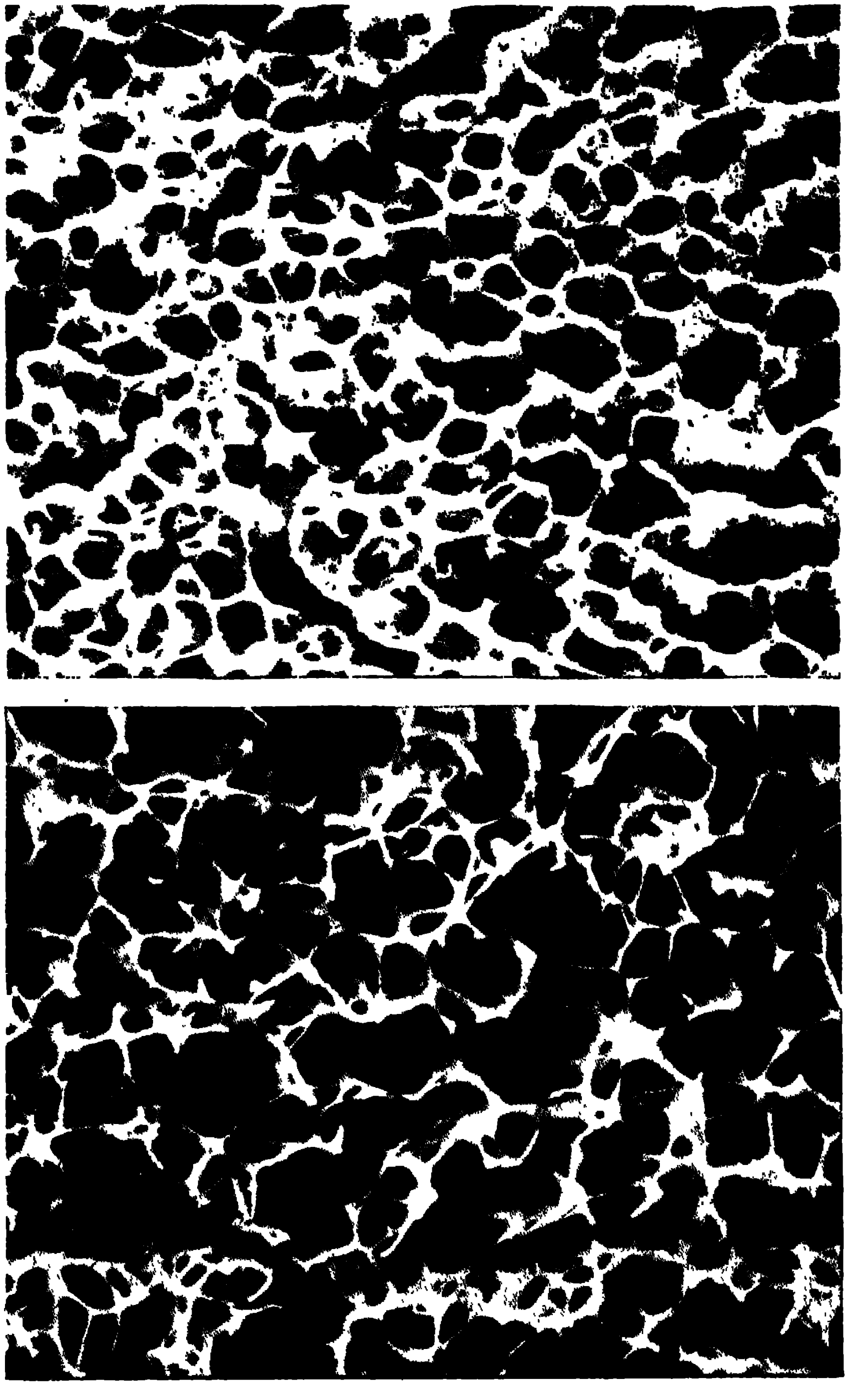

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Figure 50. Photographs of horizontal sections through: (top) normal medullary bone; (bottom) medullary bone from a patient with osteoporosis

serum levels. He described four theories of aetiology: dietary deficiency of calcium; deficient calcium absorption (e.g. in achlorhydria); dietary deficiency of protein; and gonadal hormone deficiency.

In osteoporosis the serum chemistry is usually normal. Urinary calcium excretion is said to be normal in those with gonadal hormone deficiency but Nordin (1961) reports a high urinary calcium excretion in some cases and a strikingly low excretion in others. The clinical features of osteoporosis are minimal or absent unless the weakened bone fractures. Gradual vertebral collapse may lead to low back pain, kyphosis and decrease in height. Sudden vertebral collapse frequently occurs.

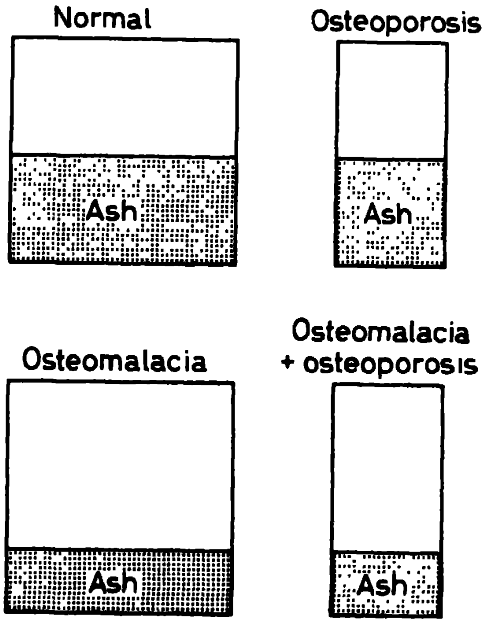

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Figure 51. Diagrammatic representation of principal metabolic abnormalities of skeleton

The radiological features are loss of bone density, due to a loss of trabecular bone and thinning of cortical bone. In severe cases the diagnosis can confidently be made on these appearances, but in milder cases this is unreliable. The ash content of bone can be reduced by a half before any radiological change is detectable, so that some objective sensitive and repeatable method of radiological assessment is required for early detection. Nordin and colleagues (1962) have attempted such an accurate assessment by means of densitometry of a lateral tomogram of the lumbar spine compared with a simultaneously exposed standard bone. While detection of mild and moderate changes is difficult, advanced gross disease has certain characteristics which are easily recognized: collapse of the dorsal vertebrae, bi-concave dorsal vertebrae (*Figure 52*) and spontaneous rib fractures. The loss of trabecular bone results in a marked

Figure 52. Osteoporosis after gastrectomy with vertebral biconcavity and collapse

contrast between cortical and medullary shadows, in contrast to osteomalacia in which there is an overall demineralization and a homogenous ground glass appearance.

PARATHYROID HYPERFUNCTION

Primary hyperparathyroidism is occasionally complicated by peptic ulceration and an aetiological relationship has been suggested (Donegan and Spiro, 1960; Chodek and Attie, 1961). If a patient with latent hyperparathyroidism and peptic ulcer is subjected to partial gastrectomy, bone disease may follow. The continuing parathyroid overactivity may be a slow cause of this disease, but it is possible that in some cases the operation may contribute a further embarrassment to bone metabolism. The following case is an example of parathyroid adenoma, associated with some signs of osteomalacia.

Case 1.—Mrs A. W., a 49 year-old housewife, was admitted to hospital with a diagnosis of primary hyperparathyroidism. The first signs of any skeletal abnormality had been noticed 26 years previously. Due to a contracted pelvis, she had two pregnancies terminated by Caesarean section at the ages of 23 and 32 years. At the age of 40, after five years typical ulcer dyspepsia, she had a Billroth I seven-tenths gastrectomy performed for active gastric and healed duodenal ulceration. A fractional test meal at this time showed no free acid. The operation cured her abdominal pain but six weeks later she began to complain first of backache and later of pains in her legs and chest. These pains became progressively more severe and she noticed increasing muscle weakness. She also observed that her height was decreasing. Three years after operation she was a semi-invalid and was confined to a wheelchair.

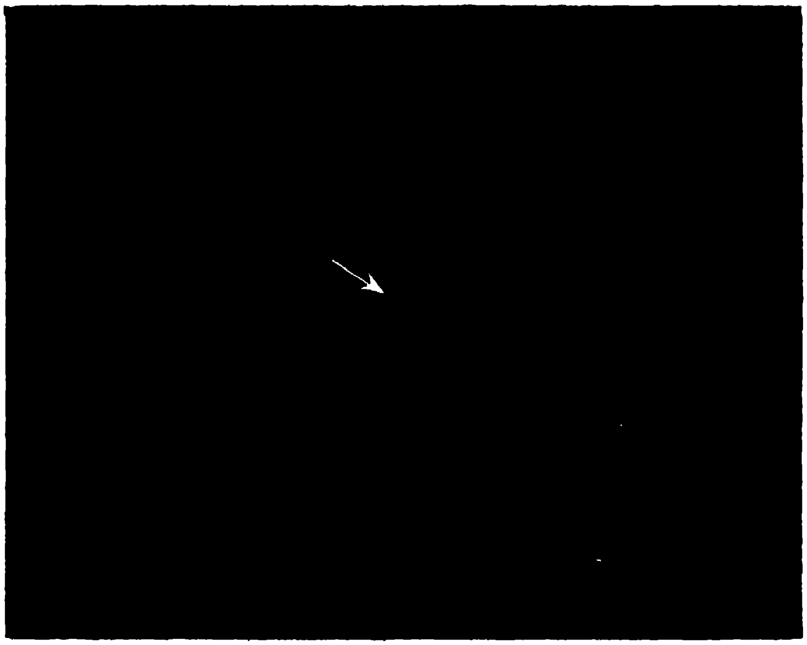

Figure 53. Subperiosteal erosion of the middle phalanx of the middle finger (arrow)

At the time of admission she appeared undernourished with a severe kyphoscoliosis and 'pigeon' chest. There was also muscular weakness so that she could walk only a few yards with a waddling gait. She had anorexia and constipation.

Investigations—Serum calcium 11·9 mg per cent; serum phosphorus 2·5 mg per cent; alkaline phosphatase 30 King-Armstrong units; blood urea 39 mg per cent; urine calcium 123 mg/day; creatinine clearance 114 ml/min; phosphorus excretion index + 0·38; faecal fats 1·1 g/day; and jejunal biopsy normal.

X-rays—X-rays showed characteristic changes of hyperparathyroidism with subperiosteal erosions in the mandible and phalanges (*Figure 53*), cystic areas in both ilia, collapsed vertebrae and deformed rib cage and pelvis.

Bone Biopsy—From the iliac crest, bone biopsy showed the characteristic histological picture of osteomalacia with osteoid seams greater than 40 μ in diameter. There were no signs of increased osteoclastic activity. Despite the histological diagnosis of osteomalacia the radiological and biochemical findings suggested a diagnosis of primary hyperparathyroidism and an exploration was made to seek a parathyroid adenoma. No tumour was found in the neck, but after splitting the sternum a benign parathyroid adenoma 5 × 4 × 5 cm was found in the upper mediastinum.

Secondary hyperparathyroidism has been described in patients with osteomalacia and steatorrhoea (Davies, Dent and Willcox, 1956). In one of our patients recorded below (*Case 5*) the radiological and biochemical findings suggest osteomalacia, yet on bone biopsy there was excess osteoclastic activity, suggesting hyperparathyroidism.

BONE DISORDERS AFTER GASTRECTOMY IN ANIMALS

The nutritional effects of total gastrectomy on experimental animals have been studied by Ivy (1940). He reported that no bone changes were observed in adult animals after gastrectomy but that, in growing puppies, total gastrectomy with oesophagoduodenostomy invariably produced generalized osteoporosis with bone deformity and occasionally spontaneous fractures, although there was no radiological evidence of rickets. Addition of soluble calcium salts to the diet caused a marked, but not complete, amelioration of the bone disorder (Bussabarger, Freeman and Ivy, 1938). They concluded that the effects of the operation were due to a combination of three factors:

(1) The absence of HCl, which normally renders less soluble calcium salts soluble and diffusible.

(2) The removal of the reservoir and triturating effect of the body and antrum of the stomach so that there is an increased speed of passage through the upper small bowel.

(3) The presence of a post-cibal acidosis ('acid tide'), which tends to decrease calcium retention (Bussabarger, Freeman and Ivy, 1938).

Later studies were reported from the same centre by Freeman and colleagues (1943) using the same operation in growing monkeys. The monkeys also showed bony changes and retardation of growth but, unlike the puppies, they developed radiological and histological signs of rickets (osteomalacia). After gastrectomy in the monkey the serum calcium and phosphorus levels fell below normal, and there was a marked elevation of the alkaline phosphatase levels. In puppies the serum levels were usually normal. No comparisons were made of the level of fat absorption in the two species.

The effects of total gastrectomy were observed in the growing rat by Johnston, Nevin and Welbourn (1960). There was a significant retardation of skeletal growth and this was not corrected by the administration of growth hormone. The type of bone disorder causing impaired skeletal development was not stated.

From these studies we may conclude that, in growing animals (monkeys, dogs and rats), total gastrectomy produces an inevitable and significant retarding effect on skeletal development. The type of resulting bone disorder is not constant, resembling osteomalacia in the monkey and osteoporosis in the dog. The predominant metabolic defect is probably a defect of calcium absorption.

BONE DISORDERS AFTER GASTRECTOMY IN MAN

Reported Series

From the Continent of Europe and from Latin America have come several reports of series of patients with bone disorders following partial gastrectomy.

Udaondo and Castex (1947), from Buenos Aires, reported 41 patients with bone disorder after partial gastrectomy; 39 showed radiological evidence of loss of bone density of the types seen in osteoporosis; this was moderate in 12 and 'intense' in 3. Although there were no clinical or radiological stigmata the biochemical findings, including a depression of the serum calcium and phosphorus and elevation of the serum alkaline phosphatase levels, supported the diagnosis of osteomalacia. Some of the bone disorders occurred in agricultural workers, but the more severe changes were seen in those who, like nuns, avoided exposure to sunlight.

From France have come three reports of a comparatively large series of patients with this syndrome. Hillemand, Mialaret and Boutelier (1960), reviewing 86 patients after gastrectomy, found 39 with bone disorders. Louyot, Mathieu and Gaucher (1961) studied

50 patients who had previously had a gastric resection and who were admitted to a rheumatic clinic (they were presumably, therefore, a selected group because of their presentation with bone and joint symptoms). They found 37 (74 per cent) with bone disease; 4 had classical osteomalacia with the Milkman–Looser syndrome, and 33 had a mixed picture of disordered bone metabolism, of whom 5 had a predominantly osteoporotic picture and 28 had abnormalities which were presumably of the osteomalatic type.

Lichtwitz and colleagues (1961a), in an extensive and detailed biochemical investigation of 42 patients after gastrectomy, found evidence of disordered bone metabolism in every patient. In 15 the diagnosis could be made on clinical or radiological grounds, in 13 a diagnosis was possible on the findings of abnormal serum levels of calcium phosphorus and alkaline phosphatase, while in 14 patients the diagnosis of abnormal bone metabolism was made only on the evidence of low urinary calcium excretion, abnormal retention on calcium infusion tests or on an abnormal calcium balance.

In a recent paper from Denmark, Harvald, Krogsgaard and Lous (1962) described their studies in 38 patients after partial gastrectomy and in a control group of 13 non-operated patients of the same age group with gastric or duodenal ulcers. They considered that a low 'net 12 hour urinary excretion of calcium' (Nordin and Frazer, 1956) was indicative of osteomalacia; they found a significant abnormality in 16 (34 per cent) of the post-gastrectomy patients and a slight abnormality in only 2 of the control group. Of the gastrectomy patients, 31 per cent had a raised serum alkaline phosphatase level, and there was a significant correlation of the serum alkaline phosphatase level with the net 12-hour urinary calcium excretion.

These relatively large series are in marked contrast to the paucity of reports from English and American centres. Table 12 summarizes most of the cases reported in detail in the literature, and it will be seen that these reports are generally of patients who have presented with gross bone disorders many years after operation. The more sensitive the tests applied for the detection of disordered bone metabolism after gastrectomy, the higher seems to be the incidence of abnormality.

Incidence

The impression gained from the study of the case reports in Table 12 is that bone disease is a rare complication of partial gastrectomy and yet, from the French and Danish series (Hillemand, Mialaret and Boutelier, 1960; Louyot, Mathieu and Gaucher,

TABLE 12

Authors	*Sex*	*Ulcer* *	*Age at operation* years	*Type of operation*	*Time interval* years	*Serum Ca mg/100 ml*	*Inorganic P mg/100 ml*	*Alkaline phosphatase*	*Units* †	*Associated abnormalities*						*Remarks*
										Steatorrhoea	*Percentage of fat absorption*	*Fe deficiency*	*B_{12} deficiency*	*Radiological diagnosis* ‡	*Biopsy diagnosis* ‡	
Sarasin (1941)	F	G	47		12					yes		yes				
	F	G	40		20					yes		yes				
Groult (1945)	F		23		17									O.M.		
Nordin and Fraser (1956)				G.E.		7·5		8·6	K.A.					O.M.	O.M.	
Langeron and colleagues (1956)	F				10											
Pyrah and Smith (1956)	F	G	38	BI	15	10·1	2·7	28	K.A.	yes	63	yes	yes	O.M.	O.M.	
Baird and Oleesky (1957)	F	G	56	BI	15	8·7	2·5	31	K.A.	yes	68	yes	yes		O.M.	
	F	D	57	BI	3	10·2	2·8	38	K.A.					O.M.	O.M.	
	F	G	67	BII	4	7·6	2·3	18·6	K.A.	yes	75	yes	yes	O.M.		
	M	D	11	G.E.	10	6·2	4·8	29	K.A.	yes	87	no		R.		Healed rickets.
	F	D	51	BI	2	9·0	2·7	40	K.A.	yes	39	no		O.M.		Chronic pancreatitis.
Ellman and Irwin (1959)	F	G	47	BI	7	8·7-10·3		12·3-22·4	K.A.	yes	84	yes		O.P.		
Mellick and Benson (1959)	F	G	38		3	7·2		12·9	Bo.	no	92·5	yes	yes	O.M.		
	F	D	40	BI	7	9·1		13·6	Bo.	no			yes	O.M.		
Hillemand, Mialaret and Boutelier (1960)	F	G	55	BII	10	8·1	3·0	49	Bo.	yes	66	yes	yes	O.M.	O.P	Cured by conversion to Billroth I.
Harvald, Krogsgaard and Lous (1962)	M	D	33	BII	11	8·0	3·0	15–19	K.A.	yes				O.M.		
	F	D	41	BII	7	7·6	3·1	15–19	K.A.	yes				O.M.		
	M		61	G.E.	5	8·4	3·1	16·2	K.A.					O.M.		
Klipstein (1962)	F	D	67	BII	15	9·2	2·4	16	K.A.	yes	85	yes	yes	O.M.	O.M.	
Welbourn (1962)	M	St.	55	BII	29	8·2	2·8	26	K.A.	no	95	yes	yes	O.M.		

* G = Gastric ; D = Duodenal; St. = Stomal. † K.A. = King-Armstrong Units; Bo. = Bodansky units. ‡ O.M. = Osteomalacia; O.P. = Osteoporosis ; R. = Rickets

1961; Lichtwitz and colleagues, 1961b; Harvald, Krogsgaard and Lous, 1962), it appears that this is a common complication. The four large series just mentioned are all of selected cases and there is no attempt, in any of them, to assess an incidence of this complication. It is of interest to note, however, that in the series of Harvald, Krogsgaard and Lous (1962) 12 of the patients were unselected in that they were studied while in hospital for conditions entirely unrelated to their gastric surgery. In five (41·5 per cent) there was a low calcium excretion as estimated by the net 12-hour urinary excretion after calcium infusion (Nordin and Frazer, 1956).

In our series of 126 unselected patients after partial gastrectomy we have estimated the alkaline phosphatase level and found, in 28 (22·2 per cent), an abnormally high level, i.e. 14 King–Armstrong units or above (unpublished data).

Time Interval

The interval between operation and presentation, in most of the patients in whom gross bone disease has been discovered, is more than five years. In those patients who have presented earlier than this there is usually some evidence of a pre-existing disorder, such as pancreatic insufficiency, which may have been at least partially responsible for the bone disease (Baird and Oleesky, 1957).

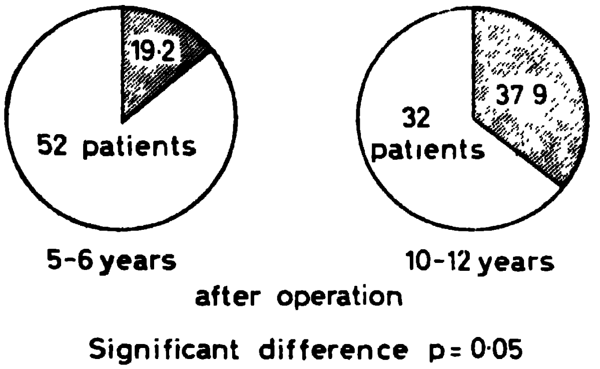

Figure 54. Percentage of patients with alkaline phosphatase of 14 K.A. units per 100 m or above after Billroth II operation

The patients reviewed in our series were taken from two groups, one of patients operated on 5–6 years before, and the other of patients operated on 10–12 years previously. There is a significantly higher incidence of high phosphatase levels in the second group (*Figure 54*). The significance of an elevated serum alkaline phosphatase level in the diagnosis of post-gastrectomy bone disorder is discussed on p. 215.

Harvald, Krogsgaard and Lous (1962), however, found no significant correlation when plotting the results of the net 12-hour urinary excretion of calcium against time interval after operation. An abnormally low calcium excretion test result probably indicates minor degrees of calcium depletion, while a raised alkaline phosphatase level may indicate active bone re-absorption occurring after prolonged calcium deficiency.

Type of Bone Disease

Post-gastrectomy bone disease is usually reported as being osteomalacia. Almost all the reported cases show biochemical features which suggest the diagnosis of osteomalacia, having low serum levels and low urinary excretion of calcium, occasionally having low serum phosphorus levels and, most frequently, elevation of the serum alkaline phosphatase level. Calcium infusion tests usually indicate calcium deficiency. When performed, bone biopsy examinations have shown thickened osteoid seams in many cases (Baird and Oleesky, 1957; Klipstein, 1962), but not in all (Welbourn, 1962). In many of the advanced cases classical radiological stigmata are present (Udaondo and Castex, 1957; Louyot, Mathieu and Gaucher, 1961; Lichtwitz and colleagues, 1961a).

In most cases there is evidence of steatorrhoea (see Table 12). Many authors have therefore likened the bone changes to those seen in sprue and gluten enteropathy and have considered that the important aetiological factor is post-gastrectomy steatorrhoea (Pyrah and Smith, 1956; Baird and Oleesky, 1957).

There are, however, certain important differences between post-gastrectomy bone disease and the osteomalacia of classical vitamin D deficiency, or of sprue, for post-gastrectomy cases do not all present with typical osteomalacia. The three cases described in detail by Harvald, Krogsgaard and Lous (1962) are classified as osteomalacia as a result of the biochemical findings, and yet the description of the radiological changes are in keeping with a diagnosis of osteoporosis. All show loss of mineralization of the vertebrae and vertebral collapse with no report of any Looser's zones.

In the French reports (Hillemand, Mialaret and Boutelier, 1960; Louyot, Mathieu and Gaucher, 1961; Lichtwitz and colleagues, 1961b) there is reference to cases described as osteoporosis or of a predominantly osteoporotic type of bone disease.

The following is a description of a patient with osteoporosis occurring after gastrectomy.

Case 2.—In 1951 Mr R. E., at the age of 52, had a Billroth II partial gastrectomy for duodenal ulceration. Since then, his weight had decreased from 154 lb. to 133 lb. In 1954, because of bilious vomiting and weight loss, he had a conversion operation from Billroth II to Billroth I. His weight was now 104 lb. and his haemoglobin 100 per cent. The symptoms were relieved but he did not gain weight. His appetite was never good, and he took little milk; his estimated daily calcium intake was over 400 mg but at times it may have been less. In 1957 he fell and fractured his right femoral neck; one year later he fractured the shaft of the same femur and in 1959 he fractured his wrist. In 1961 he was referred to an orthopaedic surgeon with increasing kyphosis and shortness of breath. X-rays showed marked osteoporosis with fractures of two ribs and collapse of D. 8, D. 12 and all the lumbar vertebrae bodies (see *Figure 52*).

He was not anaemic but had macrocytosis without a megaloblastic bone marrow (haemoglobin 14·2 g per cent; M.C.V. 112 μc; serum B_{12} 148 $\mu\mu g$/ml). The serum levels of calcium, phosphorus and alkaline phosphatase were normal, but the serum albumin level was persistently low at between 3·2 and 4·0 g/100 ml. The 24-hour urinary calcium excretion varied between 200 and 250 mg/day. A bone biopsy showed no evidence of hyperparathyroidism or osteomalacia. Mean faecal fat excretion estimated over 10 days was 2·7 g/day.

Summary. Severe osteoporosis with fractures in an undernourished man of 62 with hypoproteinaemia ten years after a Billroth II partial gastrectomy (seven years after it was converted to a Billroth I operation). There was no radiological, histological or biochemical evidence of osteomalacia; he did not have steatorrhoea and he did not now have a duodenal by-pass operation.

In our opinion the two pathological bone conditions, osteomalacia and osteoporosis, which may occur alone or together in patients after partial gastrectomy, should not be regarded as two separate diseases but as the end result of the interaction of numerous factors. For these reasons we advocate that the syndrome be referred to as ‘post-gastrectomy bone disease’, a term which is specific aetiologically, but not pathologically.

AETIOLOGY OF POST-GASTRECTOMY BONE DISEASE

After gastric operations in general, and after partial gastrectomy in particular, there is probably some deficiency of intake or absorption of calcium and vitamin D, and possibly also of protein (see p. 235). The theoretical effects on bone metabolism of gastric operation have been discussed on p. 194 and the following observations are based on data from our own patients and those reported in the literature.

Inadequate Intake of Calcium

Clark, Crookes and Mitchell (1962) have found that many patients with post-gastrectomy bone disease have a deficient dietary intake of calcium. Our own observations suggest that, in some cases, there is a general reduction of dietary intake (see *Cases 2, 4, 6* and *7*), and in some a specific reduction in milk intake (*Case 7*). However, there was a normal dietary intake of calories, milk and fats in two patients (*Cases 3* and *5*).

Inadequate Absorption of Calcium

The possible causes of impairment of calcium absorption are discussed on p. 195. It is possible to observe the effects of some of these factors including:

(1) Hypoacidity. In 25 of our patients with vagotomy alone (see p. 270), there was some evidence of disordered bone metabolism in 3 (12 per cent). In all these patients there was adequate dietary intake, and it is possible that gastric hypoacidity is the important aetiological factor. Nevertheless, the presence of normal gastric acidity is not a guarantee against the occurrence of bone disorders, since a patient is recorded by Harvald, Krogsgaard and Lous (1962), in whom a gastro-enterostomy with persistent high gastric acidity was associated with the clinical and biochemical signs of osteomalacia.

(2) Duodenal by-pass. Almost all the reports in the literature refer to bone disorders occurring after Billroth II gastrectomy or gastro-enterostomy. However, in three of the patients examined by Harvald and colleagues (1962) the operation was of the Billroth I type and in one of these the 'net 17-hour urinary excretion of calcium was only 3 per cent, indicating an extremely active osteomalacic process'. In our patient (*Case 2*) with osteoporosis there was a gastro-jejunal anastomosis for only three years followed by a gastro-duodenal anastomosis for seven years.

A comparison of the alkaline phosphatase levels in 93 patients 5–6 years after partial gastrectomy, shows no significant difference between the incidence of levels of 14 or more King–Armstrong units/100 ml in those who had a Billroth I operation compared with those who had a Billroth II anastomosis (*Figure 55*).

There is a significant difference, however, between the incidence of abnormal phosphatase levels between patients who had a vagotomy alone 13–14 years previously, and those who had a Billroth II partial gastrectomy 10–12 years before (*Figure 56*).

We have so far studied too few patients who have had a Billroth I operation more than ten years previously to make any valid comparisons.

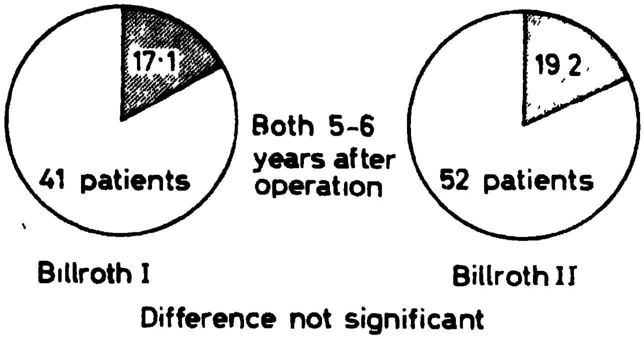

Figure 55. Percentage of patients with serum alkaline phosphatase levels of 14 K.A. units per 100 ml or above

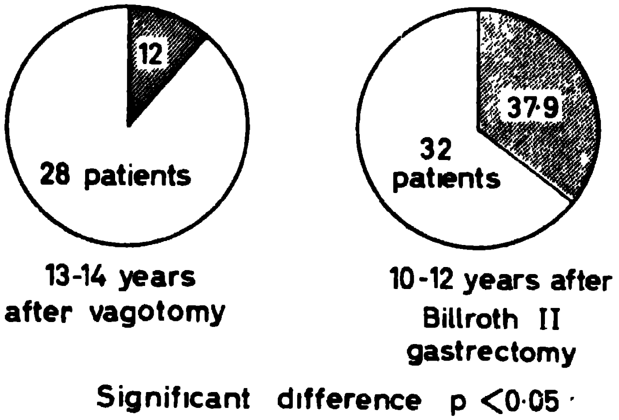

Figure 56. Percentage of patients with alkaline phosphatase of 14 K.A. units per 100 ml or above

Vitamin D Deficiency and Steatorrhoea

Many authors (Pyrah and Smith, 1956; Baird and Oleesky, 1957; Ellman and Irwin, 1959) have attributed post-gastrectomy bone disorders to calcium and vitamin D deficiency as a result of steatorrhoea; indeed most of the reported cases do have steatorrhoea (see Table 12). However, one patient of Mellick and Benson (1959) had osteomalacia and no steatorrhoea, and a similar lack of association has been found in other patients (Harvald, Krogsgaard and Lous, 1962; Welbourn, 1962; Clark, Crookes and Mitchell, 1962).

It is possible that these patients had an intermittent impairment of fat absorption and that they were in a remission at the time of investigation.

Case 3.—In 1952 Mrs R. A., at the age of 41, had a Billroth II type of operation for simple gastric ulcers. When reviewed 11 years later she had no complaints apart from mild distension after meals. Since operation she had maintained a good appetite, ate normal meals and did not avoid exposure to sunlight. Milk or milk products were not avoided and her weight had increased from 98 to 121 lb. in 11 years. Her bowel actions were occasionally loose and occurred once or twice a day.

On examination there were no physical or radiological abnormalities. Haemoglobin 14·0 g per cent, with no evidence of iron or vitamin B_{12} deficiency. The only biochemical abnormality detected was a persistently raised serum alkaline phosphatase of 20 King–Armstrong units. There was no evidence of osteitis deformans. An out-patient faecal fat estimation showed an excretion of 3·5 g/day. The diagnosis of osteomalacia was confirmed on iliac crest bone biopsy when the osteoid seams were found to be 20–30 μ in thickness.

Summary. Asymptomatic osteomalacia occurring 11 years after a Billroth II operation in a woman who had no malnutrition, anaemia or steatorrhoea, and who had a normally balanced diet and normal exposure to sunlight.

Case 4.—A Billroth II eight-tenths partial gastrectomy was performed on Mr J. T. D. for simple gastric ulceration in 1950 when he was 53 years old. During the subsequent 11 years he gradually lost weight and strength and his appetite was impaired. The onset of aching pains in his shins and low back caused him to seek medical advice in 1961. There was marked pallor, koilonychia and some peripheral hyperaesthesia but no rombergism or long tract neurological signs. Tenderness was present over the tibiae, lumbar spine and ribs.

His haemoglobin was 5·6 g/100 ml, and mean corpuscular haemoglobin concentration 24 per cent. His serum vitamin B_{12} was 65 $\mu\mu$g/ml, and the bone marrow showed occasional megaloblasts.

Radiography of the skeleton showed several un-united fractures of the ribs with poorly calcified callus. The pelvis, long bones and spine showed a complex cancellous architecture with a low mineral content; the contrast between cortex and cancellous bone was diminished. This combination of changes produced a ground-glass appearance to the skeleton characteristic of osteomalacia; there were no pseudo-fractures to be seen. Bone biopsy was not performed, but the serum chemistry was consistent with the diagnosis of osteomalacia: serum calcium 8·7 mg/100 ml and phosphorus 3·2 mg/100 ml, although the serum alkaline phosphatase was only 11·25 units/100 ml. Urinary calcium excretion was not estimated. There was no diarrhoea and the faecal fat excretion varied between 3 and 7 g/day, estimated on three separate three-day stool collections while on a 70 g fat diet. He was treated with iron and vitamin B_{12} and made a rapid return to haematological normality. His bone pains disappeared within one week of beginning treatment with calcium gluconate (1·2 g three times per day) and calciferol (50,000 units twice per day). Within six months there was radiological evidence of union of the fractured ribs (*Figure 57*).

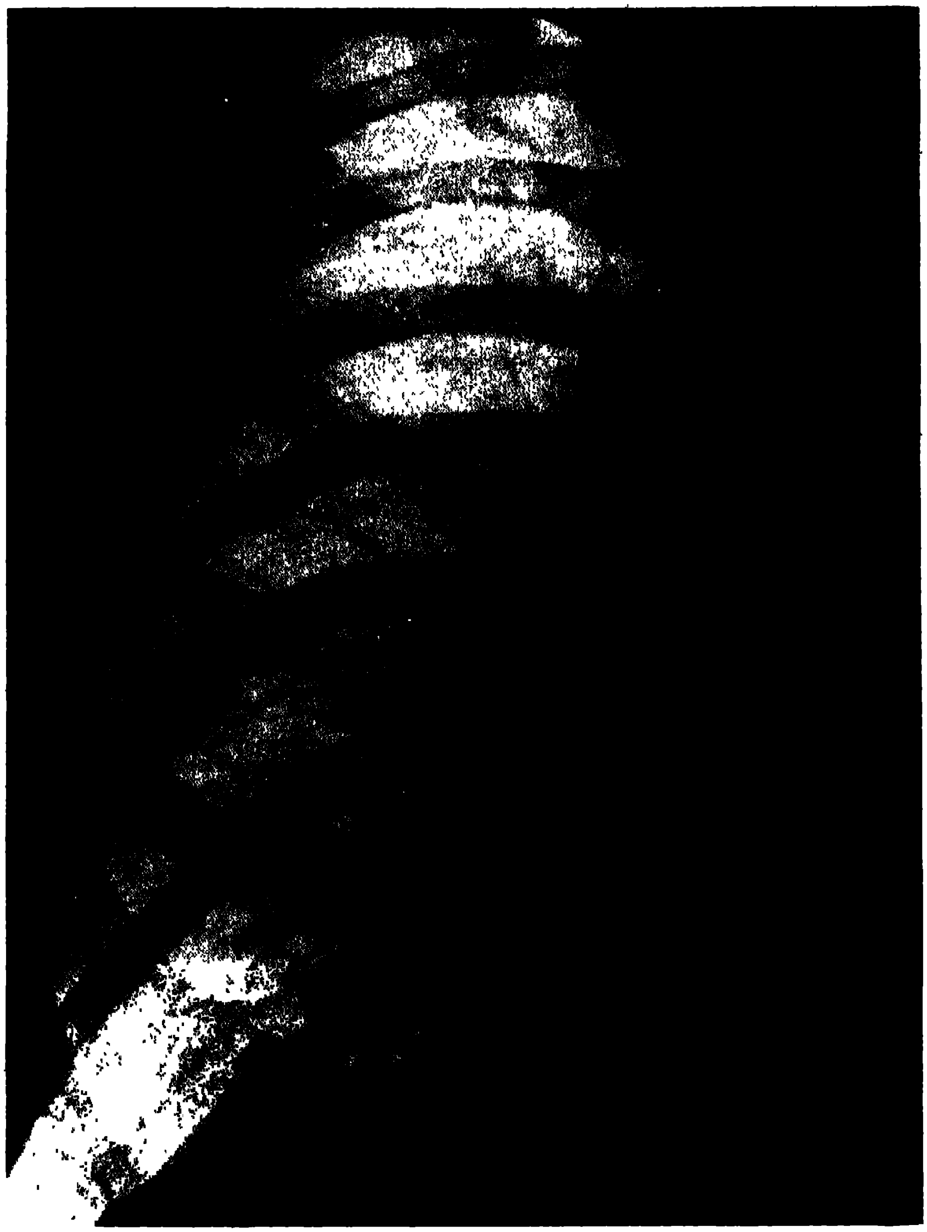

Figure 57. Healing rib fractures in patient with post-gastrectomy bone disease (Case 4) after 3/12 treatment with oral calcium and vitamin D

Summary. Osteomalacia with bone pain occurring 11 years after a B II gastrectomy, associated iron and vitamin B_{12} deficiency, but with no steatorrhoea. Rapid symptomatic and radiological response to treatment with calciferol and calcium.

Case 5.—In 1944, at the age of 35, Mr N. A. F. had a Billroth II gastrectomy for duodenal ulcer. Apart from distension after meals he was well for five years, after which time he noticed a gradual onset of weakness and cheilosis. Latterly, he noticed pains in his legs. Because of this onset of vague limb pains he was referred to an orthopaedic surgeon, who diagnosed osteomalacia on the radiological findings of Looser's zone (*Figure* 58).

Figure 58

Apart from pallor, there was no detectable abnormality on physical examination. He had microcytic anaemia (Hb 10·5 g/100 ml, M.C.V.

70 μ^3) and there was evidence of iron deficiency (serum iron 17 μg/100 ml, total iron binding capacity 506 μg/100 ml) and a low serum vitamin B_{12} level (105 $\mu\mu$g/ml). The serum biochemistry showed normal calcium (9·5 mg/100 ml) and phosphorus (3·2 mg/100 ml), but the serum alkaline phosphatase was 15 K.A. units. Urinary calcium excretion was 126 mg/day. He had normal bowel action once a day, but steatorrhoea was discovered as a result of a three-day faecal fat estimation performed as an out-patient while he was taking his normal diet (14·6 g of fat per day). Iliac crest bone biopsy showed osteoid seams which were only slightly thicker than normal—up to 20 μ in thickness. Decalcified sections showed osteoclastic activity indicating secondary hyperparathyroidism.

Summary. Osteomalacia presenting 18 years after a Billroth II gastrectomy in a man with anaemia of the predominantly iron deficiency type, who had a moderate impairment of fat absorption. X-rays showed the classical radiological features of osteomalacia (Milkman-Looser syndrome), despite normal serum and urinary calcium levels and only a slight abnormality of serum alkaline phosphatase and bone histology.

It may be argued that the absorption of vitamin D is more readily impaired than that of simpler dietary fats; also, that the dietary requirement of vitamin D is much greater when the patient has to rely upon jejunal rather than duodenal absorption (Lichtwitz and colleagues, 1961a).

Deficient absorption of vitamin A (another fat soluble vitamin) has been reported by Althausen, Uyeyama and Loran (1960) in 24 of 27 cases studied after Billroth II gastrectomy. On the other hand, in a case of post-gastrectomy osteomalacia described by Ellman and Irwin (1959) vitamin A absorption was normal, although the patient had mild steatorrhoea (84·1 per cent fat absorption on a 36 g/day diet).

Adequate exposure to sunlight should prevent the occurrence of vitamin D deficiency and if this were the only aetiological factor it should also prevent post-gastrectomy osteomalacia. Many of the reported gross examples of this disorder have occurred in patients who avoided exposure to sunlight, such as women members of religious orders (Groult, 1945; Udaondo and Castex, 1947; Louyot, Mathieu and Gaucher, 1961). However, other patients have similar post-gastrectomy bone disorders but have a presumably adequate exposure to the sun (Udaondo and Castex, 1947; see *Case 4*).

Associated Deficiencies

In many of the patients reported in the literature the presence of post-gastrectomy bone disease is associated with that of other deficiency states, in particular, deficiencies of iron and vitamin B_{12}.

The patients described by Pyrah and Smith (1956) and Klipstein (1962) and the patient of Professor Welbourn are typical examples. We have recently investigated three patients who are typical examples of the multiple deficiency syndrome (see Table 12 and *Cases 4, 5* and *6*). Despite the common finding of multiple deficiencies, some patients have post-gastrectomy bone disease with no anaemia and no evidence of iron or vitamin B_{12} deficiency (*Case 3*). In the group of 25 patients studied 13–14 years after vagotomy alone, 3 had raised serum alkaline phosphatase levels, but in none was there evidence of anaemia (see Chapter 11, p. 270).

Sex Incidence

Of the reported patients summarized in Table 12, 79 per cent are women. In the series of Lichtwitz and colleagues (1961b) 69 per cent of women are included in the group with advanced bone disease, compared with only 20·7 per cent of men. The frequent occurrence of post-menopausal osteoporosis in women suggests that if they suffered some embarrassment to their calcium or vitamin D metabolism, they might be more likely to develop bone disease than men. The calcium drain which occurs with pregnancy and lactation must add a further burden to the female patient. Two of the cases reported here (*Cases 2* and *6*) have had two pregnancies, although neither had a long lactation.

The possible ill-effect of pregnancy in exacerbating post-gastrectomy bone disease is illustrated in the following case.

Case 6.—Mrs M. H. (nulliparous) had a Billroth II partial gastrectomy in 1953 at the age of 27 for duodenal ulcer. Since then she has had a poor appetite and had eaten little but bread and milk for some years before she was seen again in 1961, by which time she had lost 13 lb. in weight. There was marked iron and vitamin B_{12} deficiency (R.B.C. 2·05 million; haemoglobin 8·5 g/100 ml, M.C.V. 128 μ^3). She had no limb pains but her serum alkaline phosphatase was 17 K.A. units. After six months treatment with iron and vitamin B_{12}, her anaemia improved (R.B.C. 4·21 million; haemoglobin 12·4 g/100 ml; M.C.V. 89 μ^3), and she then became pregnant. She was lost from our care until we heard of her delivery of a healthy child in another hospital. The confinement was complicated by septicaemia. At that time she was not anaemic because she had continued iron and vitamin B_{12} supplements, but her serum alkaline phosphatase was now 21 K.A. units, and a bone biopsy showed thickened osteoid seams indicating osteomalacia.

Summary. Osteomalacia associated with iron and vitamin B_{12} deficiency developing eight years after a Billroth II gastrectomy. The osteomalacia may have been aggravated by a subsequent pregnancy.

DIAGNOSIS OF POST-GASTRECTOMY BONE DISEASE

Patients with gross disease, such as the cases reported in Table 12, are usually readily diagnosed on their radiological and biochemical findings, even though their symptoms may be relatively mild and vague. However, it is desirable to find some means of establishing a diagnosis of post-gastrectomy bone disease before the occurrence of serious consequences, such as spontaneous fracture or vertebral collapse. Our search for the most reliable practical test for establishing an early diagnosis still continues, and at the time of writing we are unfortunately not able to give a firm unequivocal answer to the problem. Some of the possible tests are now given.

X-Rays

Pathological fractures and pseudo-fractures (Looser's zones) occur late in the disease. There are no early signs of loss of bone density for, as Lachman (1955) said, 'there is no radiological evidence of osteoporosis until 30 per cent or possibly 50 per cent of the calcium is removed from the bone'. The accurate quantitative spinal densitometer of Nordin and colleagues (1962) is the most advanced step in the logical direction. Serial x-rays of a patient's lumbar spine after gastrectomy, with the use of a bone standard or bone wedge, may provide a fairly early means of detecting bone disease.

Serum Chemistry

Reference to Table 12 shows that most of the advanced cases showed depression of the serum calcium level and that all showed elevation of the serum alkaline phosphatase level. In three of the cases reported here [*Case 2* (with osteoporosis) and *Cases 3* and *7*] the serum calcium and phosphorus levels were within the normal range. In a recent report of 100 unselected cases studied five years after gastrectomy (Jones and colleagues, 1962), we published the distribution serum calcium, phosphorus and alkaline phosphatase levels compared with a group of normals of the same age and sex distribution (*Figure 59*).

Only seven patients had a serum calcium level below 9·0 g/100 ml, and all of these had other evidence of bone disease. The serum calcium and phosphorus levels are, in our experience, unreliable as an index of early bone disease. An abnormal elevation of the serum alkaline phosphatase level, on the other hand, is a more sensitive index, as we have already shown.

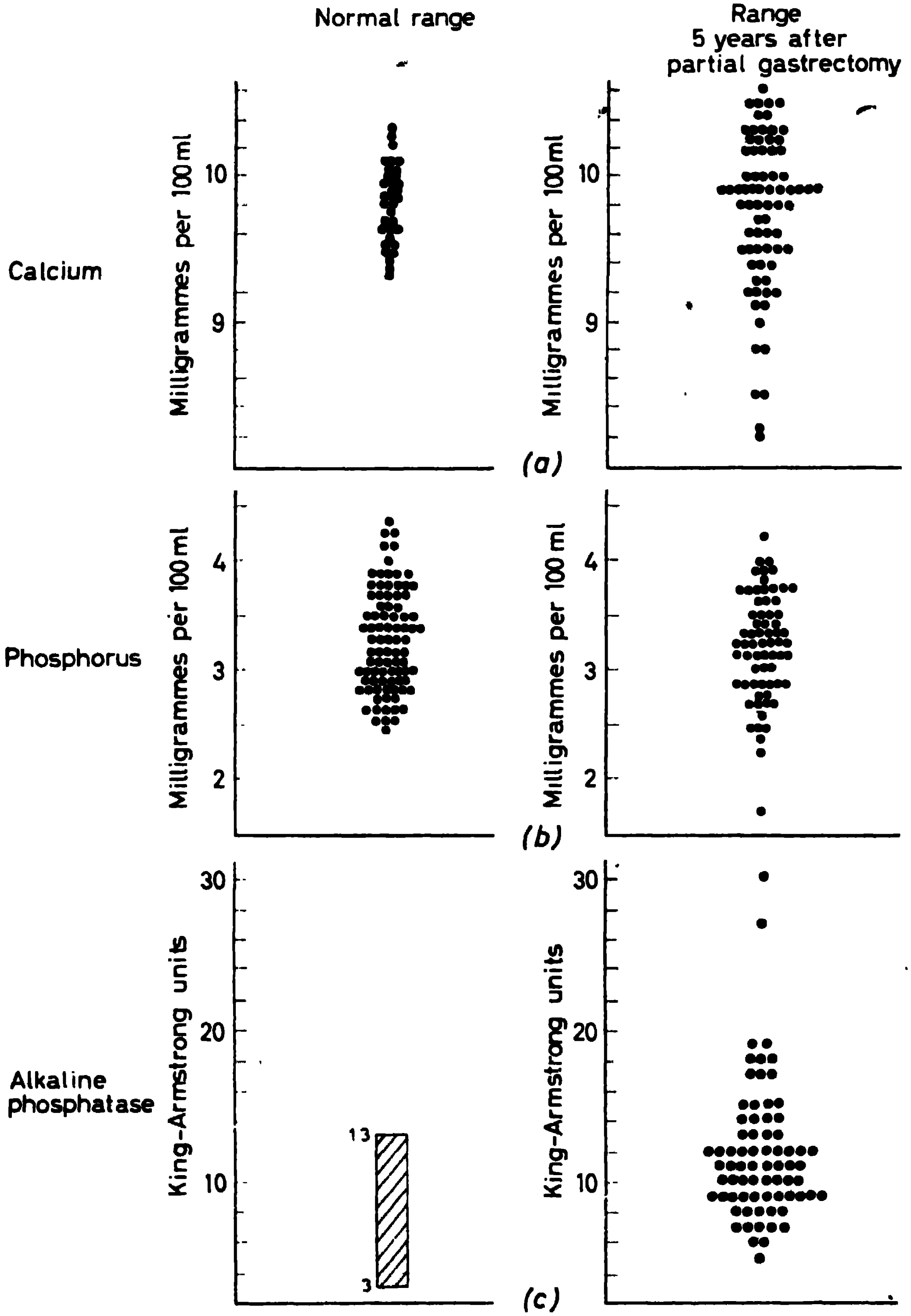

Figure 59. The range of serum levels from normal hospital and staff controls compared with the levels in 100 unselected patients 5–6 years after partial gastrectomy: (a) calcium; (b) phosphorus; (c) alkaline phosphatase

We have taken a level of over 13 K.A. units/100 ml as an index of abnormality, although the work of Dent and Harper (1962) suggests that it might be more accurate to consider 10 or 11 units as the upper limit of normality in women.

Case 7.—Mrs V. M., in 1957 at the age of 30, had a vagotomy and gastro-enterostomy for duodenal ulcer. Because of stomal obstruction this was converted, one month later, to a 40 per cent gastric resection with a gastro-jejunal anastomosis. When reviewed five years after operation she said at first that she had no complaints, but later admitted to having poor energy and appetite for about a year. She admitted noticing pains in her legs at night. Milk had upset her ever since her operation and she now avoided it. She ate meat, eggs, vegetables, cheese and bread, but in reduced quantities since her operation. She had diarrhoea with loose bowel actions 3–4 times a day. She was a housewife with two children, aged 10 and 12, and she did not deliberately avoid exposure to sunlight. She had irregular, scanty periods.

She had lost 16 lb. since her operation. Haemoglobin 6·8 g per cent, M.C.V. 68 μ^3 and M.C.H.C. 24 per cent. There was gross iron deficiency but no vitamin B_{12} deficiency; 4-day faecal fat excretion (on her usual diet) was 11·7 g/day. Stool testing for occult blood was negative on three occasions.

There was no radiological evidence of osteomalacia, but there was some loss of bone density, particularly noticeable in the pelvis but not in the hands. The diagnosis of osteomalacia, suspected on the history of bone pain and poor dietary intake, was thought to be unlikely, after the initial biochemical estimations. The serum levels were: calcium 9·7 mg per cent; phosphorus 3·6 mg per cent; and alkaline phosphatase 2 K.A. units.

However, iliac crest bone biopsy on 16.4.62 showed osteomalacia with osteoid seams 40–60 μ in thickness There was no osteoporosis (grade 9 on Beck-Nordin scale). Urine calcium excretion was low at 34·8 mg/day. At no time were the serum calcium or phosphorus levels abnormal.

Summary. An association of iron deficiency and osteomalacia five years after vagotomy and antrectomy with gastro-jejunostomy in a young woman who had an inadequate dietary intake and moderate steatorrhoea. Of particular interest here is that the serum alkaline phosphatase level, which was abnormally low when she was first seen, rose rapidly after iron therapy to levels compatible with the histological diagnosis (*Figure 60*).

From our experience in this case we suspect that there may be factors present in patients with multiple post-gastrectomy deficiencies which may depress osteoblastic activity artificially and, consequently, the serum alkaline phosphatase level. It is of interest to note that the phosphatase level in *Case 4* with gross bone disease was only 11·25 K.A. units/100 ml. In this patient, also, there was severe iron deficiency. High serum alkaline phosphatase levels may occur in conditions other than post-gastrectomy bone disease. We have seen patients in whom this syndrome was suspected because of a raised phosphatase level but who were found to have osteitis deformans (Paget's disease). This is often difficult to diagnose and must always be kept in mind. Cholestatic liver disease must also be excluded.

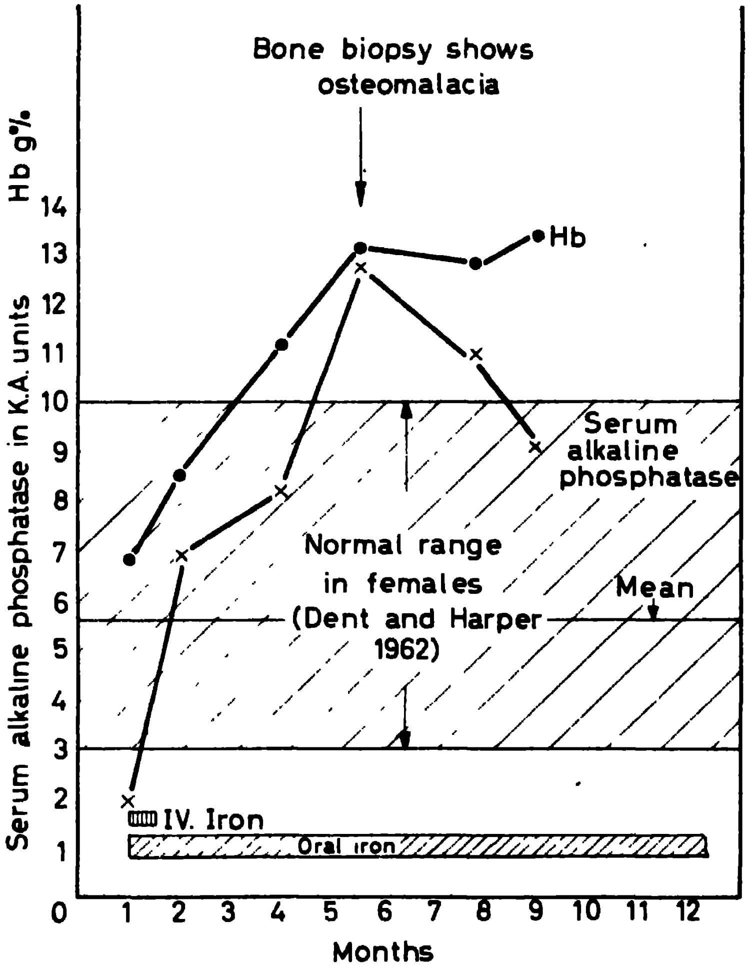

Figure 60. A rising serum alkaline phosphatase level co-incident with the successful treatment of an iron deficiency anaemia in a patient with osteomalacia (Case 7)

Bone Biopsy

In the search for a more sensitive index of early post-gastrectomy bone disease we have explored the use of an iliac crest drill biopsy. A technique has been developed which has enabled us to use this investigation as a simple out-patient procedure. A description of the technique is given on p. 222.

The examination of un-decalcified sections prepared by the method of von Kossa has enabled us to confirm the diagnosis of osteomalacia in patients in whom the suspicion was raised by the finding of an elevated alkaline phosphatase level (*Cases 3* and *6*). The work of Ball (1960) suggested that when bone is examined by this method the normal thickness of osteoid seams on the trabeculae does not exceed 12 μ. Our observations so far indicate that a wider variation of osteoid seam thickness may be found in normal people. Of 12 normal control biopsies taken from patients in the age group 33–57 we found osteoid seams up to 15μ thick in 4, and in 8 there are small areas where seams could be found of up to 32 μ in thickness. These latter are thicker than those seen in a patient (*Case 5*), who had classical radiological osteomalacia.

Our present view is that the histological examination of osteoid seams is not a reliable means of detecting early post-gastrectomy bone disease.

Radio-isotopes

Calcium^{45} has been used to study calcium metabolism but its value is limited by the long half-life of the isotope; this limits the doses which may safely be used (Bauer, 1958). By this means, and also with the aid of complex mathematical formulae, it has been calculated that there are, within the body, three different pools of exchangeable calcium which equilibrate at different rates: a large relatively fixed pool and a smaller relatively exchangeable pool within the bone, and the readily exchangeable pool in the extracellular fluid (Milhaud and Aubert, 1958). The use of ^{45}Ca in the study of alimentary absorption of calcium is limited by the marked normal variations which may occur hourly, daily or even seasonally. Aubert and Milhaud (1960) claim to have measured both intestinal absorption and intestinal secretion of calcium using ^{45}Ca. Now that the isotope ^{47}Ca, which has a short half-life, has become available it may be possible to extend the usefulness of radio-isotope studies in this field.

SUMMARY

Gross metabolic bone disease may occur as a result of some upper gastro-intestinal operations. Nevertheless, examples of gross bone disease are not commonly seen after partial gastrectomy; however, if a careful search is made it is very common to find patients with disordered bone metabolism.

Some patients with gross bone disease after gastrectomy have the classical stigmata of osteomalacia, while others have radiological and histological changes characteristic of osteoporosis. It seems likely, however, that the majority of the reported cases have a combination of both osteoporosis and osteomalacia. If it is difficult to categorize, accurately, patients with gross bone disease, it is even more so to classify the disease process in patients with minor abnormalities of bone metabolism. In view of the difficulty of classification we suggest the use of the term 'post-gastrectomy bone disease'.

Deficiencies of calcium and vitamin D are the most important aetiological factors in this disorder. These deficiencies may be due to inadequate intake or impaired absorption. General inadequacy of food intake is common after partial gastrectomy and, in addition, patients often avoid foods which are the principal dietary sources of calcium and vitamin D (e.g. milk and fats).

Impaired absorption of calcium may follow gastric operations because of the consequent hypoacidity, loss of the 'hopper' mechanism and, with a gastro-jejunal anastomosis, by-passing of the duodenum. Impairment of the absorption of fat soluble vitamin D may be due to the same factors which lead to the impaired absorption of other dietary fats after gastrectomy (e.g. pancreatico-cibal asynchrony, see pp. 74 and 249).

Most patients with post-gastrectomy bone disease, particularly of the osteomalacic type, have impaired fat absorption but there is no direct relationship between the incidence of osteomalacia and the severity of steatorrhoea. There are, in fact, examples recorded of osteomalacia occurring without demonstrable steatorrhoea.

The diagnosis of post-gastrectomy bone disease is often difficult since the symptoms develop only late in the disease and, when present, they are usually ill-defined. The relatively uncommon cases of gross osteomalacia or osteoporosis can usually be readily diagnosed on x-ray and bone biopsy. These methods, however, are not suitable for the detection of early bone disease. Possibly the most sensitive screening test for detecting this disorder is the 'net 12-hour calcium excretion test', or one of its variations. These tests reflect the body's avidity for calcium and a high proportion of positive results may be expected, for it is likely that most patients who have had partial gastrectomy will, at some time, show evidence of calcium depletion. Of the simple routine laboratory tests, an estimation of the serum alkaline phosphatase level and the 24-hour urinary calcium excretion test are the most satisfactory in detecting the presence of established post-gastrectomy bone disease.

This syndrome cannot necessarily be excluded by the finding of a normal serum alkaline phosphatase level, nor can it be diagnosed with certainty by the finding of an abnormally high level since raised alkaline phosphatase levels may occur in other unrelated conditions. A depletion of the serum levels of calcium and phosphorus may be detected in patients with gross disease, but these estimations are often of no value in the early detection of abnormality. The iliac crest bone biopsy, a safe and simple procedure, has a limited place in the routine detection of this syndrome and time-consuming calcium balance studies are impracticable as screening tests. There is therefore no simple and completely reliable test for demonstrating the presence of calcium and vitamin D deficiency in patients after gastrectomy. The most important factor in the early diagnosis of this syndrome is an awareness of the likelihood of its occurrence. Where facilities for detailed study are not available a therapeutic trial with oral calcium and vitamin D therapy may be a practical alternative.

In the treatment of established gross bone disease after gastrectomy there is good indication to treat each case as if it were a combination of osteoporosis and osteomalacia, using anabolic steroids in addition to calcium and vitamin D. It must be emphasized that there is often an associated iron and vitamin B_{12} deficiency.

In view of the probable high incidence of this syndrome after gastrectomy, the logical approach is to give prophylactic therapy in order to prevent its occurrence (for suggested dosage see p. 296).

The duty of the surgeon is to select an operation which will cause the least disturbance of calcium and vitamin D metabolism. In our opinion, vagotomy and pyloroplasty is superior in this respect to partial gastrectomy, particularly of the Billroth II type.

TECHNIQUE OF BONE BIOPSY

Percutaneous drill biopsy of the iliac crest can safely and readily be performed on an ambulant out-patient without preparation or premedication. With an apprehensive or very obese patient we sometimes prefer to keep the patient in hospital for 4–6 hours and to premedicate with an opium derivative 30 min before the biopsy.

The technique used is a modification of that described by Sacker and Nordin (1954) using a bone drill manufactured by Edwards Surgical Supplies Ltd* (*Figure 61*) (Williams and Nicholson, 1963). Two sizes of drill are available (5 and 8 cm internal diameter).

The patient lies supine on a firm couch. It is more convenient for the right-handed operator to drill the left iliac creat. The skin is anaesthetized 1 in. posterior to the anterior superior iliac spine as is, also, the periosteum over the site of the biopsy. A dental syringe containing 2 ml of 2 per cent Lignocaine and adrenalin is convenient for infiltration of the periosteum. A skin crease incision

* Edwards Surgical Supplies Ltd, 289 City Road, London, E.C.1.

8–10 mm in length is made over the iliac crest to allow the biopsy drill to be inserted. The assembled drill is pressed through the subcutaneous fat down to the bone. To prevent the drill slipping off the bone while the cortex is being cut, the centre pin is fixed into the bone by striking it lightly with a mallet. The left hand then presses the toothed outer case firmly on to the bone; this prevents the overlying periosteal and fascial fibres from becoming wound round the drill and avoids the need to incise and elevate the periosteum. The entangling of the drill by fibrous tissue is further prevented by using a to-and-fro rotatory movement as the middle or cutting part of the drill is gripped by the projecting flanges with the right hand and bored slowly into the bone. The drill is designed to cut a core of bone 10 mm long; the medullary cavity is usually encountered after about 7 mm and at this point the patient may experience some dull discomfort. If the drill is then moved slowly the softer bone can usually be cut without causing undue discomfort. To withdraw the core of bone the whole drill is loosened by rocking the base of the instrument. Once having removed the instrument the plug of bone is ejected from the drill by the central pin. There is no need to suture the skin incision and a small pressure dressing is applied. The patient is then given a mild analgesic by mouth and may return home.

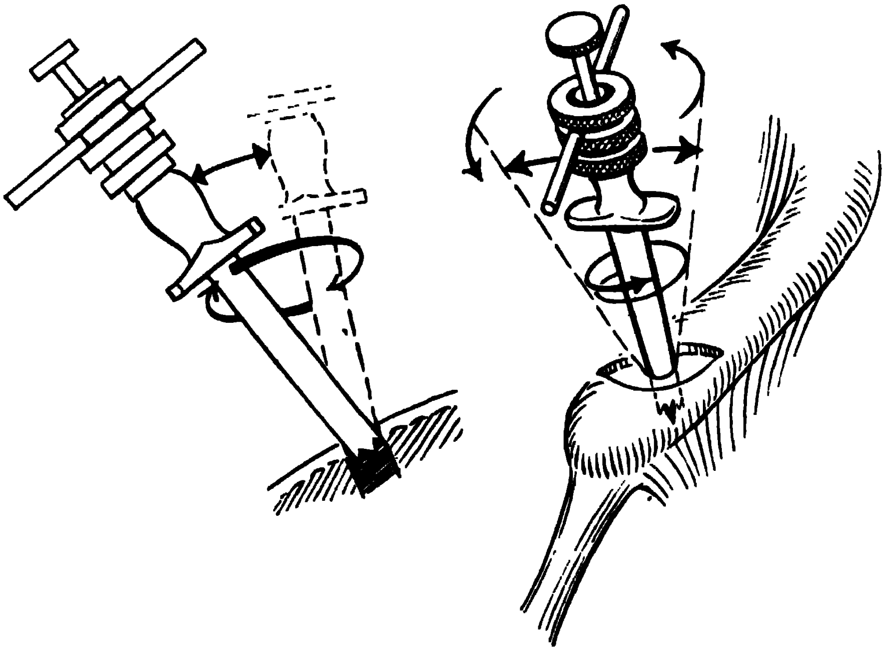

Figure 61. Bone drill manufactured by Edwards Surgical Supplies Ltd

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10

UNDERNUTRITION, MALNUTRITION AND MALABSORPTION AFTER GASTRECTOMY

J. M. French and C. W. Crane

WEIGHT LOSS

The cardinal sign of undernutrition is weight loss. If the diet is insufficient, fat and protein stores in the body are catabolized, and loss of protein is more serious than loss of fat. Keys and colleagues (1950) considered that, in semi-starvation, nitrogen loss was of great importance since it was equivalent to loss of functioning tissue mass (e.g. muscle), whereas fat loss, although greater on a percentage basis, was of little consequence functionally.

In a survey of 17 different investigations Wallensten (1954), found that the incidence of weight loss varied from 10 to 75 per cent. One of the difficulties in assessment has been the finding of a satisfactory criterion for loss of weight. A comparison of pre- and post-operative weights, which has been used most frequently, can be most misleading. Taking two obvious examples, a patient with pyloric obstruction, vomiting, dehydration and marked weight loss, will gain weight after operation regardless of the type of anastomosis, whereas a patient who is overweight before operation because of high caloric intake from special diets, e.g. extra milk and cream, will lose weight.

Loss of weight after operation was recorded in 47 per cent of 864 Billroth II cases (collected from the earlier literature) by Ivy, Grossman and Bachrach (1950); Rauch (1952) found that 80 per cent of 699 Billroth II patients could not maintain their pre-operative weight. Anderson, Gunn and Watt (1955), working in Illingworth's clinic, found that 55 per cent of 315 men and 65 per cent of 51 women remained below their pre-illness weight after Billroth II gastrectomy. Brookes, Waterhouse and Thorn (1960) found that in 722 patients with peptic ulcer (gastric and duodenal) 59 per cent were below their 'ideal' weight one year after partial gastrectomies of various types.

In the literature on partial gastrectomy, opinions are divided as to the extent of the weight loss after different types of anastomosis.

Series of Billroth I and II (Polya) cases have been compared from this point of view (see Table 13).

Comparison of the results between retro-colic and ante-colic Billroth II gastrectomies do not appear to have been made, but the studies of Butler (1961) suggest that such a comparison might well give valuable information.

TABLE 13

Loss of Weight After Billroth I and II Compared

Authors	*Billroth I*		*Billroth II*	
	Total number of patients	*Patients who lost weight* per cent	*Total number of patients*	*Patients who lost weight* per cent
Meurling (1953)*	77	18	101	21
Wallensten (1954)	114	5	182	13
Zollinger and Ellison (1954)†	31	33	101	65
Harkins and Nyhus (1956)	529	42	135	74
Postlethwait and colleagues (1961)†	12	33	98	43

* Compared with 'average' weight before operation (not immediately before).
† Weight loss determined by reference to 'expected' weight from standard tables.

Everson (1952) reviewed the literature on nutrition after total gastrectomy and concluded that all patients had lost weight after operation, regardless of the type of anastomosis. Ellison (1955), in a series of ten total gastrectomies showed that all had lost weight, no difference being found between those with oesophago-duodenostomy and those with oesophago-jejunostomy.

Despite the different methods of computation, it seems clear that weight loss is common after partial gastrectomy, but is even more common after the Billroth II operation. Whether there is a difference between the short post- or longer ante-colic anastomosis is not known. After total gastrectomy, weight loss invariably takes place.

It is not easy to determine the exact causes responsible for the loss of weight after gastrectomy in all cases. The following factors must be considered: lowered caloric intake from simple lack of appetite, or that due to symptoms or fear of symptoms after meals; decreased absorption due to incomplete digestion or to defects in the absorptive mechanisms; defective or abnormal utilization. In some patients, more than one of these causes may be operative.

In total starvation the fat stores become depleted, and the tissue proteins of the body become the currency for energy production. In semi-starvation a generous supply of calories, in the form of fat and carbohydrate, may diminish the ensuing nitrogen loss from the body (Smith, 1926), but when the supply of calories is deficient despite otherwise adequate protein intake, weight loss and a negative nitrogen balance are inevitable until a new nitrogen equilibrium is established at a reduced level of overall metabolic requirement.

It is probable that the most important single cause of failure to regain or maintain weight after partial gastrectomy is simply diminished caloric intake. If the patient can be persuaded to eat sufficient food then his weight will increase (Johnston, Welbourn and Acheson, 1958). MacLean and colleagues (1954) considered that weight loss after partial gastrectomy in two patients could be accounted for by a daily food intake of between 20 and 40 per cent less than before operation. A Report of the Committee on Nutrition (1950) has accepted that the caloric requirements of average adult males and females are 2,200 and 1,800 cal/day, respectively. Johnston, Welbourn and Acheson (1958) estimated that, in a group of patients underweight following sub-total gastrectomy, reduction in food intake provided 24 per cent less calories than was theoretically necessary to maintain normal weight and that the deficiency could be as great as 600 cal/day. The symptoms responsible for lack of appetite or fear of eating are discussed in Chapter 4 and will not be further considered here.

MALABSORPTION

Defective digestion and absorption result in an increased output of nutrient materials in the faeces and a loss of calories. Wollaeger and colleagues (1946) reported faecal losses of food material equivalent to between 122 and 673 cal/day in some patients after gastrectomy while Randall (1954) and Ellison (1955) showed that, by this means, the caloric intake may be depressed below 1,400 cal/day. Ellison (1954) estimated that a loss of 7,300 cal/month in the faeces from malabsorption would represent a loss of 16 lb. of body weight over an interval of 15 months.

The methods employed in the elucidation of the influence of gastrectomy on digestion and absorption are similar to those used in the investigation of diseases involving lack of digestion (e.g. pancreatic disease) with diminution or absence of the external pancreatic secretion, or malabsorption disease (e.g. idiopathic steatorrhoea).

Of the three main constituents of food, apart from water, fat alone passes through into the faeces relatively undestroyed by bacteria. Although its chemical constitution may be altered by intestinal bacteria (James, Webb and Kellock, 1961) as well as by digestion, fat is easily extracted and estimated quantitatively, and the endogenous component in faeces is small.

Protein is attacked by the resident intestinal flora, particularly in the colon; it can be estimated crudely only as total nitrogen, and here the endogenous component may be large. Carbohydrates, in the form of starches and sugars, are attacked strongly by bacteria and degraded to a variety of end-products. There are no practical means of detecting failure of carbohydrate absorption by faecal examination except by microscopy for starch granules and estimation of volatile fatty acids, which are some of the bacterial breakdown products of the sugars and dextrins. Neither of these methods is of any use for the quantitative study of unabsorbed carbohydrate. Because of these difficulties, excretion studies of food unabsorbed after gastrectomy have almost been limited to fat and nitrogen. Both direct and indirect methods have been used.

FAT

Excretion

Many investigations have shown that after subtotal gastrectomy, steatorrhoea is commonly present; after total gastrectomy it is almost invariably so. Early direct studies on faecal fat which indicated this (Gordon-Taylor and colleagues, 1929) relied on the measurement of the percentage of fat in dried faeces. This method of assessment is now recognized as open to a high degree of error and it was not until metabolic balances were used that the extent and frequency of fat absorption defects were clearly established (Gavrila and Danicico, 1929, Rekers, Pack and Rhoads, 1943; Wollaeger and colleagues, 1946).

The last-named group of workers and Ellison (1955) and Butler (1961), showed that there was a better absorption of fat after Billroth I subtotal gastric resection than after Billroth II, and the contention of Stammers (1955), that steatorrhoea is more likely to occur in patients with long ante-colic loops than in those with short retro-colic loops, has been confirmed by the work of Butler (1961), who also showed that shortening the long ante-colic loop will diminish the frequency and degree of steatorrhoea significantly.

These valuable studies are supported by other less extensive reports (Wollaeger, 1950; Robins, Robertson and McIntosh, 1957;

Main, Scott and Gobbell, 1960). The importance of the type of anastomosis is confirmed by animal work; Everson (1954) showed that, in dogs, twice the normal amount of fat was found in the faeces after Billroth I operations, and five times the normal amount after Billroth II. Hertel (1930) operated on dogs to make Billroth I and Billroth II anastomoses and thereafter made fistulas to the abdominal wall from the middle or end of the small intestine. Determinations of fat, nitrogen and glucose were made on the intestinal contents delivered through the fistulas and the total absorption of the ingested food was calculated.

In the upper part of the digestive tract there was a very low absorption in both BI- and BII-operated dogs. In the end-fistula of the small intestine, the absorption values for the BI-operated-dogs were nearly normal. In the BII dogs the absorption was incomplete for fat, protein and glucose. These experiments are open to the criticism that intestinal motility may change after fistula operations.

After total gastrectomy there is generally an excess of fat in the faeces and the quantity increases with the intake (Rekers, Pack and Rhoads, 1943), although the percentage of intake absorbed may actually improve. In seven total and three near-total gastrectomies, Ellison (1955) found 11–53 per cent of the fat intake in the faeces. Lawrence and colleagues (1960) found an extensive variation from 3 to 59 per cent of the fat intake as faecal fat. Although the fat output rose with increase in fat intake, the percentage absorption remained practically constant. It is interesting to note that 3 of their 25 patients had a fat absorption of more than 92 per cent. In a series of oesophago-gastrectomies, Phillips and colleagues (1961) showed that the faecal fat averaged 12–15 g/day, despite the fact that the antrum was retained in each. There was little difference in fat excretion between four different types of anastomoses employed in their proximal gastrectomies, all of which included vagotomy.

The frequency and severity of steatorrhoea after various types of operations on animals has been examined by Welbourn, Hallenbeck and Bollman (1953), Javid (1955) and Everson (1952, 1955). A strange anomaly noted by Welbourn and Doggart (1956) was that total gastrectomy with oesophago-duodenostomy in the rat leads to an improvement in fat absorption. This remains without explanation. From the various studies in the literature, as well as his own, Butler (1961) concluded that: steatorrhoea seldom occurred after gastro-enterostomy; it seldom followed vagotomy alone; it was rarer after Billroth I operation than after the Billroth II; it was almost invariable after total gastrectomy; and the addition of vagotomy to partial gastrectomy increased fat loss in the faeces.

Intubation Studies

A second method of direct study has been used by Lundh (1958) by intubation with polythene tubing, as devised by Blankenhorn, Hirsch and Ahrens (1955). He withdrew test 'meals' containing fat, protein, glucose and a non-absorbable reference substance, polyethylene glycol. Although unable to draw conclusions about the total absorption of the given meal, he was able to show that, in the Billroth II operation, the conditions were less favourable with regard to digestion and absorption of fat than in the Billroth I.

Indirect Studies

The digestion of fat has been followed by giving an oral dose to gastrectomized dogs and following the rise in blood lipid (Mineta and colleagues, 1954). The radioactivity of the serum, urine and faeces has been followed in gastrectomized man, after ^{131}I labelled olive oil and oleic acid (Shingleton and colleagues, 1957; Shoemaker and Wase, 1957; Barker, Malm and Reetsma, 1960). Unfortunately, it is now generally agreed that there is poor correlation between the results of absorption tests with radioactive fat and the simple chemical fat balance methods (Berkowitz, Croll and Shapiro, 1962), and the sole conclusion of value from this work is that after gastrectomy fatty acid is more easily absorbed than triglyceride (Ruffin and colleagues, 1958); this may be regarded as indicating that a defect in pancreatic digestion is part of the mechanism of the defective fat absorption.

From the literature, the incidence of steatorrhoea has been estimated to occur in about 60 per cent of patients (Butler, Capper and Naish, 1954). It must be made quite clear that this is usually unaccompanied by symptoms, and that diarrhoea is quite infrequently associated with it. Occasionally, the steatorrhoea may contribute to a fully developed malabsorption syndrome, with gross diarrhoea, an excess of faecal nitrogen, hypoproteinaemia, avitaminosis and anaemia (McPhee, 1953; Frankel and Moore, 1953; Naish and Capper, 1953; Bruce, 1955). The incidence of this severe state is less than 1 per cent; Bruusgaard (1946) observed only 2 patients with severe diarrhoea in 174 Billroth II gastrectomies, and in a personal series of 800 Billroth II operations, Butler (1961) noted it in only 7, all of whom had ante-colic anastomoses. The majority of these 7 developed the syndrome 7–11 years after operation. Others have noted no change, or a gradual lessening of steatorrhoea as the post-operative period extends (Welbourn, Hallenbeck and Bollman, 1953, in dogs; Brain and Stammers, 1951; Polak and Pontes, 1956; Lawrence and colleagues, 1960, in man).

The reconciliation of these divergent views may lead to an important conclusion. The lessening of the steatorrhoea after operation, noted by many, may be due to gradual compensatory improvement in the disturbed digestive and absorptive mechanisms, while the severe states, noted occasionally by Butler (1961) and others, may be due to a superimposed disorder or major derangement of the post-operative state demanding operative interference. These important complications are mentioned on p. 237 in the discussion of mechanisms causing steatorrhoea, and also on pp. 72–78.

NITROGEN

Excretion

As with fat, the only satisfactory method for determining excessive loss of nitrogen is by the balance method. In normal subjects the upper level of daily faecal nitrogen was determined by Wollaeger, Comfort and Osterberg (1947) to be 2·5 g. Despite the general picture of undernutrition after total and, less commonly, subtotal gastrectomy, surprisingly few complete nitrogen balances have been reported.

After total gastrectomy in patients, the incidence of faecal nitrogen above the upper limit of normal varied from 30 per cent of a small series of patients (Rekers, Pack and Rhoads, 1943) to 50 per cent (Schwartz, Bodansky and Randall, 1956a; Ellison, 1955; Lawrence and colleagues, 1960). On the other hand, Moreno (1956) found that only one of six patients had values greater than 2·5 g/day and, in a larger series, 17 patients had a normal faecal nitrogen (Kelly and colleagues, 1954). According to Gavrila and Danicico (1929), who were the first to make a report on this subject, faecal nitrogen excretion was increased in 8 of 13 patients after partial gastrectomy, in some as high as 4·2 g/day. This incidence approaches that for total resection but later studies have not confirmed this. For example, Wollaeger and colleagues (1946) observed that all of 14 patients with Polya gastrectomies had normal faecal nitrogen and Robins, Robertson and McIntosh (1957) found raised values in only 10 per cent of theirs.

A slightly higher incidence was found by Ellison (1955) and Lawrence and colleagues (1960), of 33 and 25 per cent, respectively. After Billroth I operations, nitrogen excretion was lower than after Billroth II and the incidence of excessive faecal nitrogen was also lower (Ellison, 1955; MacLean and colleagues, 1954), although in one series no difference was found (Robins, Robertson and McIntosh 1957). Experimental work in dogs by Everson (1954) showed less faecal nitrogen after Billroth I operations than Billroth II, which supported the conclusions of the former investigators. Although a considerable proportion of the nitrogen in the faeces of normal subjects is of endogenous origin from mucus, epithelial cells and enzymes (Lusk, 1928), the assumption is made in the gastrectomy studies that the increased faecal nitrogen is derived mainly from dietary sources.

If the diet contains excessive amounts of poorly digestible material, e.g. wheat fibre, the endogenous fraction may be increased and this might also be expected after gastrectomy when the reservoir function of the stomach is reduced or abolished and undigested food gains immediate access to the small intestine. Wollaeger (1950), Ellison (1954), Robins, Robertson and McIntosh (1957) and Lawrence and colleagues (1960) all showed that faecal nitrogen was most often increased in those with steatorrhoea, but that there was little correlation between the actual amounts of fat and nitrogen.

In some patients with total or subtotal resection, on an adequate intake of fat and protein, fat excretion was high and nitrogen normal, while in a few, stool nitrogen was raised and the fat normal. Unabsorbed fat in the alimentary canal does not seem to provoke an increase in stool nitrogen. Patients with steatorrhoea from impairment of liver function had no increase in faecal nitrogen (Atkinson, Nordin and Sherlock, 1956; Gross and colleagues, 1950) and, in gastrectomized dogs, faecal nitrogen was reduced with pancreatin, while the unabsorbed fat remained unchanged (Emery, 1935; Everson, 1952). Ellison (1955) found a tendency for faecal nitrogen excretion to increase with time after partial resection, a trend which was not observed after total gastrectomy, probably because dietary intake of both fat and protein was low, especially in the first few post-operative months.

Full nitrogen balance studies on patients after total and subtotal gastrectomy have given additional information on their nitrogen requirements (Schwartz, Bodansky and Randall, 1956a; Lawrence and colleagues, 1960). Following both types of operation an increased nitrogen intake was necessary to maintain nitrogen equilibrium, but the requirements after subtotal procedures were less than after total.

It is difficult to compare, accurately, the data reported in the different investigations since patients have been studied on diets differing widely in composition and caloric value and no attempt has been made at standardization on a body weight basis. It is possible, however, to draw some general conclusions: after gastrectomy of all types, the incidence of excessive faecal nitrogen is less than that for fat. It is greatest after total gastrectomy, less so after Billroth II operations and least after Billroth I, and the excess is derived mainly from unabsorbed dietary protein. The protein needs of patients following gastrectomy are increased, apparently in excess of replacement of the simple dietary loss in faeces, before nitrogen equilibrium is established.

Intubation Studies

Lundh (1958) examined the rate of disappearance of radioactive albumin, mixed with a standard meal, from the small intestine of patients after both types of Billroth gastrectomy. He found that the digestion of the albumin was reduced, but to a greater degree, in the Billroth II. He also noted that protein digestion and absorption were disturbed to a greater degree than fat absorption, a conclusion which is diametrically opposed to all other workers in this field. In view of this, it is unfortunate that his experiments did not include studies of the nitrogen excretion to confirm his findings. His exceptional conclusion may perhaps be explained by his use of a native protein, since it has been shown that the rate and extent of digestion of protein is influenced greatly by denaturation (Ivy, Morgan and Farrel, 1931; Bocci, 1961).

Indirect Studies

^{131}I labelling has been used to study digestion and absorption of protein by methods adapted from those used for the study of patients with pancreatic disease (Chinn and colleagues, 1952; Freeark, Kozoll and Meyer, 1957). No difference was found between gastrectomized and normal subjects by Babb and colleagues (1953) and Shoemaker and Wase (1957). However, when Shoemaker and Wase fed large quantities of horse meat, together with labelled protein, to gastrectomized dogs they were able to demonstrate impaired assimilation of the tracer material.

Richmond and Girdwood (1962) fed casein and followed the rise in concentration of blood amino acids in ten patients with Billroth II gastrectomies and found that maximal values were reached quickly and were higher than in the control studies. The same has been observed with protein hydrolysates (Johnson and colleagues, 1953) and with single amino acids (Ariel and colleagues, 1943).

Richmond and Girdwood also measured the levels of four essential amino acids, leucine, lysine, methionine and phenylalanine, in the plasma of their patients and found them consistently elevated. The significance of this has not been determined. Whether the body is unable to synthesize protein at an increased rate, and whether the excess of amino acids is converted into urea, are not known, but it seems unlikely that amino acid imbalance would result from this accelerated digestion and absorption. Following total gastrectomy there was a marked reduction in the rate of absorption of protein, and studies with ^{23}P and ^{35}S labelled materials have shown that this was greatest after oesophago-jejunostomy (Nakayama and colleagues, 1960).

Protein in Serum and Plasma After Gastrectomy

There are few reports on the concentration of serum or plasma protein. Ariel and colleagues (1943) found that the serum proteins fell rapidly immediately after operation for carcinoma of the stomach. No similar fall took place in patients after gastrectomy of the same magnitude for benign lesions, despite similar urinary losses of nitrogen; these authors, therefore, could not relate the falls in serum protein in their patients to the extent or severity of the operation. Kelly and colleagues (1954) studied 23 patients from 4 months to 8¾ years after gastric resections for carcinoma and observed that total serum proteins tended to remain low in those who survived for some time; they found 7 g per cent in 5; 6–7 g per cent in 12; and less than 6 g per cent in 6 patients. Exclusion of the stomach—and therefore of gastric digestion—in operations for oesophageal stricture was found by Callender and colleagues (1961) to lead to low serum proteins in the majority of 11 patients. They found that 8 of those with oesophago-jejunal anastomoses had a serum albumin of less than 4 g per cent.

Partial gastrectomy for peptic ulcer leads to less marked changes. Watt, Walker and Munro (1960) found no gross changes in plasma proteins, although values for total protein, albumin and alpha-2 globulin tended to be slightly lower than normal in 40 patients, ten years after Polya (B II) gastrectomy. Postlethwait and colleagues (1961) found normal total serum proteins in 98 patients examined 2–7 years after Hofmeister (B II) gastrectomy. Apart from the results in gastric carcinoma and gastric exclusion, which appear to provide special cases, the deviations of serum or plasma protein from normal values after gastrectomy are slight.

Plasma protein levels, however, do not reflect the extent of overall nitrogen loss until this assumes severe proportions. Weech, Wollstein and Goettsch (1937) fed dogs for 15 weeks with a diet deficient in protein but adequate in calories. They found that nitrogen was lost from tissue protein in a proportion of 78 per cent, from haemoglobin 19 per cent and from plasma protein only 3 per cent and this mainly from the albumin; similar results have been found in man. Human volunteers were starved until the average body weight fell by a quarter; the plasma protein levels were then compared with those at the beginning of the study and showed quite small changes (Keys and colleagues, 1950). The relatively normal values for serum and plasma after gastrectomy cannot, therefore, be taken as an effective index that patients after gastrectomy are not suffering from protein depletion; indeed, when they are low, depletion must be regarded as severe.

THE MECHANISMS OF THE ABSORPTIVE DEFECTS

Gastrectomy upsets the normal physiological processes of digestion and absorption at many points, and the mode of disruption differs according to the type and extent of operation. It is unlikely that steatorrhoea is caused by a single disturbance when the normal arrangements have been altered mechanically, anatomically, neurally and hormonally, although one disturbance may predominate in some instances. The various factors will be considered and some weight given to each, separately.

Loss of Reservoir: its Relation to Gastric Digestion and Emptying

The most important factors in determining how much of the reservoir effect is preserved after gastrectomy are the type and extent of the operation, and the design, position and size of the stoma. The more complete the gastrectomy, the smaller the reservoir and, with antral excision, this normally means the shorter the period of gastric storage (reservoir effect), unless special steps are taken to preserve or increase it. The narrowings produced by the Hofmeister–Finsterer modifications of the Billroth II procedure help, principally, to prevent food flowing back into the duodenum. Small stomal anastomoses have been designed to slow evacuation (O'Neill, 1950; Lahey and Marshall, 1952; Zollinger and Williams, 1956).

Attempts to define the gastric storage period in partially gastrectomized patients have been unsatisfactory. Radiologically, rapid emptying of a plain suspension of barium sulphate is demonstrated easily, almost regardless of the type of anastomosis. Meurling (1953) found a slower gastric emptying after Billroth I than after Billroth II gastrectomy. The difference was more conspicuous if the barium contrast was mixed with food, e.g. milk, than with water.

Schlaeger (1960) examined 65 patients with Billroth I, and ante- and retro-colic Billroth II with Hofmeister types of anastomosis, and showed that precipitate emptying occurred in each case. If the size of the fluid meal was increased, the gastric remnant served as a rapidly empyting conduit without peristaltic activity and only transient reservoir capacity. The rate of emptying was unrelated to dumping syndrome or nutritional status. Examination of the same patients on a second occasion, at which a ham sandwich was added to the meal, disclosed in many cases a striking capacity for holding particulate matter, in complete contrast to the rapid emptying demonstrated on the first occasion. He concluded that the problem could only be examined in individual cases by a radiological examination, which included food.

As well as diminishing the capacity to take a normal-sized meal, gastrectomy causes a decrease in the period of gastric storage, trituration and digestion, and a more precipitate entry of food into the small intestine without the normal regular small contributions of bile and pancreatic juice. With the stomach intact, meals containing fat are evacuated more slowly than those containing protein or carbohydrate alone.

Despite the implication that fat might need a more prolonged stay in the stomach for digestion than the other two main foods, it seems certain that gastric digestion for fat is not important, except in so far that some may be contained in lumps of other material, e.g. meat, which would normally be partially digested and liquified by gastric juice. The slow intermittent release of fatty meals through the intact pylorus, mainly mediated through the influence of enterogastrone, appears more closely related to the processes of emulsification, digestion and absorption of fats and oils in the small intestine, which are slow compared with the rate of digestion of other foods.

Unlike fat, protein undergoes some digestion in the stomach. In normal subjects, it begins there and may be extensive (Elsom, Chornock and Dickey, 1942; Nasset and Davenport, 1955; Taylor, 1961). Even native proteins, such as serum albumin, appear to undergo considerable alteration (Borgström and colleagues, 1957).

Gastrectomy reduces the amount of HCl and pepsin and the time available for peptic digestion, and Lublin (1931) regarded the increased faecal nitrogen as being due to this. On the other hand, Fisher (1954) believed that the stomach was not essential for the assimilation of protein, but these divergent views need to be amplified. The effect on protein digestion of reduction or total loss of HCl after partial or total gastrectomy is difficult to assess, but peptic activity may not be greatly altered after partial resection (Harrower, Brook and Cooper, 1956; Stubbe, 1957; Perry and colleagues, 1957).

The early studies have been reviewed critically by Lundh (1958) and Butler (1961). The effect of the changes on gastric proteolysis is particularly difficult to estimate for two reasons; first, although it is generally agreed that the optimum for peptic digestion is about pH 2, the gastric pH following meals, even in normal subjects, is usually higher than this (Beazell, 1941; James and Pickering, 1949; Borgström and colleagues, 1957); secondly, Taylor (1959) has shown that pepsin has a second optimum between pH 4 and 5, and considerable proteolytic activity can be found in gastric juice in the total absence of HCl—in pernicious anaemia, for instance. It is possible that the reduced amounts of pepsin, acting at a pH higher than normal, are sufficient to initiate the digestion of protein (Cathcart, 1921).

Such a view, however, offers no explanation for the finding that, after total gastrectomy, increases of faecal nitrogen are by no means inevitable. Ivy, Morgan and Farrel (1931) made the observation that, in their gastrectomized dogs, raw meat appeared unchanged in the stools 2–4 h after being fed, but cooked meat did not. Hertel (1930) showed that there was considerable digestion of meat in the lower parts of the intestine in his dogs. It is likely that, under these conditions, digestion is confined to proteins that have been thoroughly denatured, e.g. by cooking, and might explain the findings reported by Lublin (1931) and Gordon-Taylor and colleagues (1929) of the presence of connective tissue in the faeces of gastrectomized patients.

A further point which must be considered later (p. 242) is that gastric proteolysis may, indirectly, affect pancreatic digestion since independently from the HCl-secretin-pancreozymin mechanisms, the products of peptic digestion have been found in animals to produce the most powerful stimulant of pancreatic secretion (Wang and Grossman, 1951); peptone has been used in this way in many experimental studies. In general, the evidence suggests that at least the well-cooked denatured proteins of the western diet, eaten in normal quantities, can be assimilated without the action of pepsin.

Restoration of the Reservoir

Meals can be fed at very short intervals, as though from an external reservoir and, ignoring the question of gastric digestion, the effect is roughly equivalent to the intermittent release of food through the pylorus. Brain and Stammers (1951) showed that this procedure improved fat absorption; the intake of food can also be increased and small gains in weight may follow (Warren, 1954; Lepore, 1956). Emery (1935) showed, in two dogs with total gastrectomies which had gross malabsorption with large meals, that if the diet was fed slowly so that the food entered the duodenum at the approximate rate at which it had been shown to leave the normal dog's stomach, the absorption of fat was normal. Although useful in some instances, very frequent feeding is not really a satisfactory method of restoring the reservoir effect.

An effective way of increasing the gastric reservoir is anatomical enlargement. In one of the earliest reports it was noted that a gastric remnant of three fingers-breadth at operation had enlarged to hold half a litre of fluid 2½ years later (Schuchardt, 1895); it is a matter of common experience that both gastric remnant and that part of the small intestine to which it is anastomosed undergo compensatory enlargement from dilatation or hypertrophy. Several methods have been devised for restoring the gastric reservoir surgically: from one loop of jejunum to form a small sac (Henley, 1952; Longmire and Beal, 1952); two or three loops to form a large bag interposed between the cut end of the stomach or oesophagus and duodenum (Moreno, 1956; Hays and Clark, 1960) and in other ways (Hunt, 1952); or from ileum and colon (Moroney, 1951 and 1953; Lee, 1951). The interposition of a jejunal segment through the mesocolon, to form a connection between gastric remnant and duodenum, has more recently been used as a routine primary procedure in a series of partial gastrectomies for peptic ulcer (Hedenstedt, 1959; Annersten, 1959). Weight gains were said to be impressive and fat absorption normal, although no figures have been given. Unless vagotomy is performed at the same time, ulcers recur in a high proportion [23 per cent (Henley, 1957) 9 per cent (Hedenstedt, 1960)]. Replacement procedures have been reviewed critically by Hepp, Couinard and Bucaille (1957).

All these operations, various aspects of which are discussed elsewhere, are designed to restore reservoir capacity, but they also aim at restoring continuity of the intestinal tract in a manner similar to the Billroth I operation. Consequently, it is not possible to assess the effect of restoring the reservoir capacity alone upon absorption, since it cannot be separated from that of restoring continuity, which has been shown by Butler (1961) to be very important. Everson (1955), however, was able to show in dogs that fat excretion with jejunal replacement after subtotal gastrectomy was not significantly different from that noted in normal animals, whereas after a Billroth I operation, it was slightly higher. The size of reservoir may therefore play some part, the most important feature being a delaying action.

Restitution of 'pyloric' control has been attempted by transposition of the ileo-caecal valve isoperistaltically in dogs (Symbas, Killen and Scott, 1960). Of more interest, Willms and Jordan (1961) inserted a reversed 2·5 cm jejunal segment strategically between the gastric remnant and jejunum in six dogs. One year post-operatively, gastric meals emptied at a normal rate. Reversed peristaltic movement in the jejunal ring was visible, fluoroscopically, at laparotomy, but the reversed segment did not prevent an increased loss of fat and nitrogen in the stools after operation (Billroth II type); although it did have a significant effect upon plasma volume changes following meals of high osmolarity. A patient with severe dumping syndrome after Billroth II gastrectomy has been successfully treated in the same manner (Jordan, McIlhaney and Williams, 1962).

INTESTINAL HURRY

The abrupt exodus of food from the stomach remnant may be followed by an accelerated passsage down the small intestine especially if carbohydrate is present in large amounts. Sugars and other water soluble materials are rapidly dissolved and the solution reduced to isotonicity in the jejunum by an inpouring of fluid (Abbott, Karr and Miller, 1937; Machella, 1949) but, unless absorption keeps pace, an excessive amount of fluid accumulates and the food moves on rapidly by peristaltic waves instead of by the slower, normal process of progressive segmentation. A rapid conversion of starches to sugars and dextrins aggravates this effect and the stimulus to peristalsis may be enormous. This can be readily demonstrated and, in an extreme case, a mixture of barium sulphate and hypertonic glucose reached the caecum in 5 min (Glazebrook and Welbourn, 1952).

The duodenum has a remarkable capacity for diluting hypertonic solutions (Abbott, Karr and Miller, 1937) and, probably, normally exerts a protective effect upon the jejunum. Some have noted that although the passage through the upper intestine is accelerated, it is normal in the ileum (Bruusgaard, 1946) or there is a compensatory slowing (Moreno, 1956; Schlaeger, 1960).

In general, the observations show that small intestinal hurry, largely confined to the jejunum, hastens food away from its quota of bile and pancreatic juice, is most pronounced in the Billroth II type of operation and can be reduced by keeping starches and sugars to a minimum. Atropine and ganglion-blocking drugs, such as hexamethonium and probanthine, may reduce diarrhoea and improve fat absorption by decreasing small intestinal motility (Wollaeger, 1950; Glazebrook and Welbourn, 1952). They may, however, have an inhibitory effect upon pancreatic secretion; they have had little success in practice because absorption is not regularly improved, and they have pronounced unpleasant side effects when used in adequate dosage.

DIMINISHED FLOW OF PANCREATIC JUICE AND BILE

The presence of food in the duodenum stimulates pancreatic secretion and gall bladder contraction by several mechanisms, resulting normally in the addition of small amounts of pancreatic juice and bile to each bolus of food as it passes through the duodenum and their intimate mixture with it. If the stomach empties rapidly through the duodenum, e.g. after Billroth I, these mechanisms may not be brought fully into play, and if the duodenum is bypassed, as in Billroth II, they may fail almost entirely. The influence of gastrectomy on the pancreatic secretion has been examined experimentally by studying the pancreatic response to food and to hormonal and vagal influence separately, although it is not easy to isolate each completely from the other.

Response to Food

It has been shown in normal subjects that food in the jejunum stimulates a smaller pancreatic response than food in the duodenum, both in volume (Howard, James and Evans, 1951) and in enzyme content. After gastrectomy, Lundh (1958) found very low enzyme concentrations early in digestion in the intestine compared with the considerable concentrations found in normal subjects (Borgström and colleagues, 1957), the lowest being in the Billroth II patients, and in these the entry of bile was delayed.

Stern (1929) examined over 100 patients after Billroth I and II gastrectomy and concluded that neither operation had much effect on the secretion of pancreatic enzymes. Butler (1961) intubated patients and delivered meals into the duodenum or jejunum before and after Billroth I gastrectomy; he measured the pancreatic response and came to the opposite conclusion. He showed that although resting secretion was increased, the pancreatic response to meals delivered into the duodenum was impaired after gastrectomy and the response to meals into the jejunum was almost abolished, volume, lipase, trypsin, amylase and bicarbonate secretion being greatly reduced over a period of an hour. He also noted a delay in the appearance of the bile, confirming Lundh's observations. Studies in a patient with complete pancreatic fistula after a Billroth II gastrectomy showed first a delayed pancreatic response to meals and then a flow only for 1 h instead of several (Hirota, 1958). Experimentally, in dogs with pancreatic fistula, there was a marked decrease in the pancreatic response to ingestion of food after gastrectomy (Annis and Hallenbeck, 1952; Richman and colleagues, 1954).

Response to Hormonal Mechanism

In gastrectomized dogs, the capacity of the pancreas to secrete when stimulated with HCl or secretin was normal (Annis and Hallenbeck, 1952; Richman and colleagues, 1954). In man, secretin tests after gastrectomy were normal in the majority of patients (MacLean and colleagues, 1954; Kelly and colleagues, 1954). Dreiling (1957), who found a reduced secretin response in 4 of 12 patients with post-gastrectomy steatorrhoea, also found a reduced response in 7 of 14 patients with post-gastrectomy dumping syndrome and 14 of 52 patients with non-fatty diarrhoea. It seems unlikely, therefore, that his findings have any special significance for post-gastrectomy steatorrhoea. Nevertheless, a disturbance in the hormonal mechanisms after operation seems probable even though the pancreas can respond to secretin under test conditions. The amounts of secretin (Weaver, 1927) and of pancreozymin (Harper and Raper, 1943) found in the wall of the small bowel are maximal in the wall of the duodenum, decrease as lower levels of the intestine are reached and may be absent from the lower ileum. It may be concluded, therefore, that the lower the anastomosis, the less effective will be the hormonal stimulus to the pancreas.

Response to Vagal Influences

Partial or complete vagotomy is inherent in many types of gastric resection and, consequently, the effect of vagotomy on the pancreas has received attention. The pancreas receives a vagal innervation through the coeliac branch of the posterior vagus nerve: there are stimulatory and inhibitory fibres. Confusion in interpretation of experimental data has arisen because the stimulatory fibres to the gland may excite external secretion but, at the same time, stimulate the ducts to close, giving an apparent inhibition (Anrep, 1916). Early studies on the relationship of pancreatic function to the vagal nerves have been reviewed by Lagerlöf (1942).

Electrical stimulation of the peripheral end of the cut vagus in dogs led to an increased pancreatic response in some, and inhibition in others (Crittendon and Ivy, 1937). Harper, Kidd and Scratcherd (1959) found that stimulation of the efferent end of vagal nerves (of cats and dogs), cut within the abdomen, led to an increased output of pancreatic amylase; stimulation of the afferent end was less effective. They concluded that there was a vago-vagal reflex affecting pancreatic secretion. This finding is supported by White, Lundh and Magee (1960), who demonstrated that gastric distension in dogs led to an increase in pancreatic secretion and considered that this was mediated by a vagal reflex arc.

The results of section of the vagus have proved somewhat equivocal. Early work in dogs with pancreatic fistulae (Crider and Thomas, 1944) indicated that section of the vagi resulted in an absence of pancreatic secretion after instillation of peptone and HCl solutions into the intestine; partial recovery ensued within a few days of operation. Later and more extensive work in dogs with pancreatic fistulae (Routley and colleagues, 1952) showed that on stimulation with meat meals, HCl, secretin, pancreozymin and parasympathomimetic drugs, the volume and enzyme content of pancreatic juice was not diminished after vagotomy—in fact, there was usually a slight increase, except in the case of insulin stimulation (vagal). In chronic pancreatic fistula dogs in which the HCl-secretin mechanism was by-passed by diverting the HCl through a gastrostomy, Tankel and Hollander (1958) showed that vagotomy had no significant effect on basal pancreatic secretion (volume and bicarbonate), and response to secretin was enhanced.

In human subjects, the evidence for a change in pancreatic secretion through vagal influences is very meagre. Howard, James and Evans (1951) studied a 32-year old man with a pancreatic fistula from a bullet wound. Prostigmine increased the secretion and atropine and banthine (and ephedrine) reduced it. Banthine did not block the flow increase after secretin. Pfeffer, Stephenson and Hinton (1952) compared ten vagotomy patients with ten patients with thoracolumbar sympathectomy and ten normal subjects, by intubation methods, aspirating pancreatic secretion through a Miller–Abbott tube. They found that the vagotomized patients had a lower resting pancreatic secretion than either of the other two groups. After secretin and secretin–insulin stimulation, pancreatic secretion in the vagotomized patients fell to very low levels while in the other two groups it was considerably increased. Butler (1961) studied a small number of vagotomized patients with the duodenal and jejunal meal and found the pancreatic flow lower than normal. They had not been studied before vagotomy.

Burge (1960) held the view that vagotomy caused pancreatic deficiency in his patients and believed that this was responsible for diarrhoea (said to be steatorrhoea) seen by him in a high proportion. Selective vagotomy with preservation of the coeliac branch supplying the pancreas appeared to reduce the incidence of pale stools and diarrhoea, but later studies indicated that preservation of the hepatic branch was more essential (Burge and colleagues, 1961). The inference that selective vagotomy reduced fatty diarrhoea was unfortunately not substantiated by him, since no faecal fat determinations were carried out in either series.

Increases in volume and amylase content of pancreatic juice collected by tube after distension of the stomach in human subjects were regarded by White, McAlexander and Magee (1962) as mediated by a reflex vagal arc, since they were abolished by atropine. Dreiling (1957) examined 16 patients after vagotomy and found a normal pancreatic response to the secretin test.

Pancreatitis

Sometimes the pancreas is damaged at operation especially when it has already been eroded by peptic ulceration, or chronic gross pancreatitis may be present at operation. Acute pancreatitis rarely follows operation, the course is severe and mortality is high (Warren, 1954). Minor trauma to the pancreas resulting in the loss of small amounts of tissue is of little consequence, as far as the efficiency of digestion is concerned, provided the mechanisms for stimulating pancreatic secretion are in order, since it is well recognized that 80–90 per cent of the pancreas has to be extirpated before increases in fat and nitrogen in the faeces are noted (Vermeulen, Owen and Dragstedt, 1943).

This view is confirmed by the work of Coffey, Mann and Bollman (1940), who showed that a pancreatic fistula has to be almost complete before pancreatic insufficiency makes its appearance. The overall efficiency of the alimentary canal for the assimilation of protein is extremely high. Even after total pancreatectomy and partial gastrectomy, absorption of denatured protein is still possible

(Crane, 1961). However, pancreatitis after operation could clearly cause steatorrhoea, but occurs too seldom to be responsible for the type of malabsorption under discussion.

It may be concluded that after gastrectomy, there is a disorganization of the mechanisms governing the flow of pancreatic juice in response to food, causing incomplete digestion. Although, in the majority of patients, the pancreas itself is normal, this 'pancreaticocibal asynchrony' (Brain and Stammers, 1951) appears to be the most important single cause of malabsorption. Hormonal and afferent and efferent neural pathways are affected and the extent and seriousness of their involvement depend upon the type and extent of the gastrectomy and the position of the anastomosis.

Effect of Addition of Bile and Pancreatin to Food

Although several mechanisms may be involved in causing increased fat and nitrogen excretion in the stools of gastrectomized patients, so much evidence points to a disturbance of pancreatic digestion that it is clearly necessary to study the effect of aiding it. Observations of this nature, which include the addition of bile, various forms of pancreatic extract or stimulating the secretion or release of the patient's own pancreatic secretion by artificial means, have been very incompletely carried out.

Results which are available indicate that some improvement may be achieved. However, for a proper evaluation of the results of this work, it must be understood that in established pancreatic insufficiency (gross chronic pancreatitis or cystic fibrosis of the pancreas), it has rarely proved possible to make fat absorption normal by the oral administration of pancreatic extracts with meals, whatever the dose or type of preparation. Although some improvement often occurs it is frequently very slight, even with enormous doses of pancreatin, and the most satisfactory method so far is the administration of a potent extract hourly (Jordan and Grossman, 1959); even so, fat absorption is not restored to normal. Although this may be due to the readiness with which the enzymes are inactivated by HCl or destroyed by autodigestion, it is more probably due to the difficulty of effecting their even distribution through the food at the appropriate time and level in the intestine.

It seems most likely that pancreatic juice must be supplied continuously and under proper conditions of pH and with bile to achieve normal absorption. Similarly, the steatorrhoea of bile fistula dogs can only be corrected effectively by the continuous intraduodenal administration of bile and not by its addition with meals (Searle and Annegers, 1949).

It is not surprising, therefore, that the results of the addition of bile and pancreatin to patients with steatorrhoea after gastrectomy, on the ground of a functional pancreatic insufficiency, have been unspectacular. Rekers, Pack and Rhoads (1943) gave 25 g pancreatin to a patient with a total gastrectomy on a diet containing 60 g protein and 40 g fat. Steatorrhoea was reduced from 20 to 8 g/day and faecal nitrogen fell from 2·8 to 1·2 g, but 4 g bile salts daily caused diarrhoea and increased faecal fat from 22 to 33 g and nitrogen from 3·5 to 5 g. On the other hand, Polak and Pontes (1956) in a small series of gastrectomy cases, noted that pancreatin alone gave no improvement in fat absorption in balance tests over 12 days in seven patients, pancreatin with bile gave improvement in six, and bile alone gave a similar improvement in nine. Five of the patients had oesophago-jejunal anastomoses and four had B II gastrectomies. Less definite findings were reported by others. Everson (1952) gave 25 g pancreatin to six patients with total gastrectomies and noted a substantial decrease in fat and nitrogen loss, but five of these had also had a partial pancreatectomy. Frankel and Moore (1953) noted a striking improvement in a patient with partial gastrectomy after the inclusion of pancreatin and sodium bicarbonate with meals, but no balance data were given.

Schwartz, Bodansky and Randall (1956b) found no improvement in six cases of total gastrectomy with pancreatin using a dosage up to the equivalent of 72 g pancreatin (U.S.P.) per day. Purified lipase gave equally disappointing results. Culver (1962) added bile salts (one patient), pancreatin (four) and pancreatin plus bile (two) and found no improvement with any. Shingleton and colleagues (1957) noted that bile and pancreatin increased the level of blood radioactivity after oral administration of ^{131}I labelled fats.

In gastrectomized dogs Emery (1935) and Everson (1952) observed that pancreatin and fresh pancreas did not decrease faecal fat loss, although the faecal nitrogen was reduced.

These results are rather few and their divergence may be due to the difficulty in getting bile and, more especially, pancreatin in an active condition well distributed in the food in the small intestine. Occasionally, the addition of pancreatin and bile result in a remarkable improvement in absorption (*Figure 62*).

Emulsifying agents have been used to improve fat absorption. Tween 80 (polyoxyethylene sorbitan mono-oleate) was found to improve it in four patients with subtotal gastrectomy (Jones and colleagues, 1948). In a later report (Culver, 1962), fat absorption was improved in eight but unchanged in five. A controlled study by Badenoch, Truelove and Ward-McQuaid (1951) of Tween 80 for improving nutrition failed to show weight increases after six months treatment in five underweight gastrectomized patients, but no fat absorption data were included in their study.

Stimulation of the hormonal mechanism for pancreatic secretion before or during meals has been used by a number of investigators. Dilute HCl before meals was found to improve fat absorption (Emery, 1935; Rekers, Pack and Rhoads, 1943; Lawrence and colleagues, 1960). Glycine or orange before meals appeared to act as a direct stimulus to pancreatic secretion, whereas glutamic acid appeared to act only through the HCl-secretin mechanism; glycine and orange were given to a number of gastrectomized patients as 'pancreatic appetizers' with symptomatically beneficial effects (Hirota, 1958) but absorption data were not recorded. The injection of secretin and pancreozymin during digestion was shown to increase the absorption of ^{131}I-triolein (Johnson and colleagues, 1961).

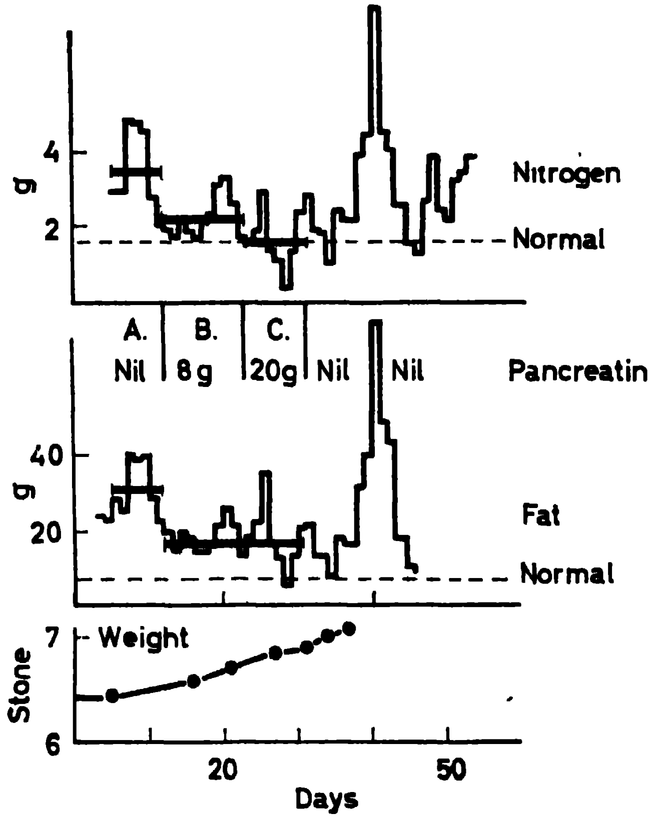

Figure 62. A 50-year old woman had persistent diarrhoea for five years after a Polya gastrectomy. The diarrhoea disappeared within 48 hours of giving pancreatin in milk with all meals. Hypoproteinaemia with oedema of the feet was corrected in two weeks and the oedema disappeared. During the periods A, B and C the patient was given a controlled diet containing 70 g fat and 100 g protein. Both fat and nitrogen excretion were considerably diminished when pancreatin was given, and increased again when it was stopped (French, unpublished)

It may be concluded that there is some improvement in absorption when digestion is assisted by the addition of pancreatin and bile. However, the field has been very incompletely explored and insufficient consideration given to achieving satisfactory mixing of the added materials. There are many unsolved problems associated with improving absorption in patients with proven pancreatic insufficiency.

IMPERFECT MIXING OF FOOD AND DIGESTIVE JUICES

From general considerations and previous discussion, it is clear that the proper mixing of food and enzyme-containing juices is very important for complete digestion. Some further aspects need to be discussed briefly. Lundh (1958), using the polythene intubation technique, found very low trypsin and chymotrypsin levels compared with normal in the distal part of the meal in partially gastrectomized patients. There does not therefore seem any great likelihood of the enzymes, secreted late in response to food, 'catching-up' the meal; the forepart may go through the intestine largely undigested unless the pancreas can be stimulated beforehand.

Attempts to improve mixing by stimulating the intestine (e.g. with cholinergic drugs) are more likely to stimulate peristaltic movements than segmental and so result in diarrhoea; no such studies appear to have been recorded.

Re-routing the food to obtain better mixing has an important place both experimentally and therapeutically. Butler (1961) showed that re-routing food through the duodenum by conversion of Billroth II to I gave better absorption of fat, although he gave no figures for nitrogen. Other operations, such as the Roux-en-Y (Schofield and Anderson, 1953), pantaloons anastomosis (Steinberg, 1949) and other jejunoplasties (Wells and Welbourn, 1951) also result in improved mixing. They have usually been carried out primarily to abolish biliary vomiting and other post-gastrectomy symptoms, however, and their effect upon those with malabsorption has not been studied.

VAGOTOMY AS A CAUSE OF ABSORPTIVE DEFECTS

There is no doubt that diarrhoea sometimes follows vagotomy; whether this indicates that malabsorption is also induced is still debatable, because there is surprisingly little information considering the supposed frequency of diarrhoea. The incidence of diarrhoea varies from 4 per cent (Kay, 1962) to 30 per cent (Burge, 1960).

In a nation-wide survey in the U.S.A. on the results of vagotomy, the Report of the Committee on Surgical Procedures (1952) noted that transient diarrhoea occurred in 4·9–19·8 per cent of patients and persistent diarrhoea in 1·6–4·4 per cent of all ulcer cases, with little difference between the various procedures, several of which included stomach drainage operations. Unfortunately, no study of the malabsorption problem was included in their report and, since the operation fell into disrepute as the sole procedure for peptic ulceration before proper investigation of this aspect, practically no figures are available.

Fox and Grimson (1950) examined nine patients by the fat balance method. In six of these a drainage operation had also been carried out and, of the remaining three, one excreted 10 g fat per day and two excreted normal amounts. Wollaeger (1961) examined two patients and found fat absorption to be normal, while Burge (1960) contended that steatorrhoea was a common sequel to vagotomy but gave no data.

Kay (1962) examined 17 patients before and after vagotomy, 9 of whom had a concomitant gastro-enterostomy and 8 a pyloroplasty. There was a mean rise in fat excretion after operation of 4·2 and 3·0 g/day in the two groups, respectively; the difference between the mean rises was not significant, and both could have been due to the drainage operation and not to the vagotomy.

In dogs, fat absorption was normal after vagotomy (Javid, 1955; Welbourn, Hallenbeck and Bollman, 1953). The little evidence available therefore indicates that steatorrhoea does not follow vagotomy alone, although the subject cannot be considered to have been examined fully, especially as a number of studies indicate that vagotomy increases the degree of steatorrhoea after both gastric resection (Ellison, 1955; Javid, 1955; Robins, Robertson and McIntosh, 1957) and gastro-enterostomy (Javid, 1955).

BY-PASSING OF THE DUODENUM

The main effects of this are inadequate mixing of food, bile and pancreatic juice and reduced effectiveness of the secretin–pancreozymin mechanism. These have already been fully considered but some other aspects deserve comment.

Autodigestion of Enzymes

When pancreatic juice is liberated into the duodenum, the trypsinogen is immediately activated by enterokinase, and trypsin may attack and inactivate all digestive enzymes, including proteolytic (Avakian, 1961), especially in the absence of competitive substrates in the form of food. Lagerlöf (1942) found that inactivation of lipase in freshly recovered duodenal juice had reached 70 per cent at 37°C in 30 min. This may explain the disparity in enzyme concentrations in the belated pancreatic response to food (Lundh, 1958; Butler, 1961). Butler noticed that the longer the afferent loop the greater the destruction of lipase and, sometimes, of trypsin. The concentrations of amylase, lipase and trypsin normally increase equally when the pancreas is actively secreting (Lagerlöf, 1942).

Afferent Loop Obstruction and Infection

Naish and Capper (1953) drew attention to the possibility of the afferent loop causing a 'blind-loop' syndrome. The loops which are formed at gastrectomy are of the self-emptying type, however, and it seems unlikely that bacterial infection of an afferent loop can play an important part in infecting the gut, unless the secretions are dammed back by some form of obstruction. One of Naish and Capper's cases was of this nature and, in this patient, the afferent loop was enormously distended. Other cases were described by Kinsella and Hennessy (1960). Two similar patients have been seen in Birmingham, in one of whom re-operation with a jejunal implant restored gut continuity and converted steatorrhoea into normal fat excretion.

Obstruction of the afferent loop, with trapping of the pancreatic enzymes, will naturally lead to a diminished pancreatic digestion of food and, in the second Birmingham case, the gross steatorrhoea which was present was of the pancreatic type, unemulsified fat being passed separately from the main bulk of the faeces. On the other hand, Goldstein, Wirts and Kramer (1961) treated two patients with this syndrome with antibiotic drugs and reduced the steatorrhoea. Bacterial counts in the afferent loop were carried out and the good results therapeutically were obtained in those in whom the loop appeared most heavily infected. Similar cases were reported by Kinsella, Hennessy and George (1961).

GASTRO-ILEOSTOMY AND GASTRO-COLIC FISTULA

Occasionally, the stomach is inadvertently anastomosed to the ileum, in some reported cases as near as 12·5 cm to the ileo-caecal valve. This accident usually results in severe diarrhoea and steatorrhoea immediately following the operation, but in several patients symptoms have developed months or years afterwards for the first time. This is because most of the food continues to pass through the pylorus instead of through the anastomosis. A feature of the barium meal is refilling of the stomach through the gastro-ileal anastomosis. Faecal vomiting may therefore be present. If partial gastrectomy is also performed, or there is pyloric stenosis, there is an immediate downhill course, resulting in the death of the patient, unless the anastomosis is taken down. The literature has been reviewed by Brown, Colvert and Brush (1947) and Moretz (1950). In one case, dense adhesions and malrotation of the gut led to the surgical error but in none of the other 24 cases reviewed (Moretz, 1950) was there a satisfactory explanation for the mistake.

Gastro-colic fistula or—as a rule and more correctly—gastro-jejuno-colic fistula, is a well recognized complication of simple gastro-enterostomy, but sometimes occurs after partial gastrectomy as a sequel to recurrent ulceration in the jejunum. The diarrhoea, steatorrhoea, hypoproteinaemia, anaemia and general malnutrition are usually severe and the condition, like gastro-ileostomy, can only be corrected by surgical intervention. It is frequently missed on barium meal examination, and only becomes evident with a barium enema. It is now generally thought that infection of the upper gut with colonic contents is more important in causing the steatorrhoea than the passage of food directly into the colon (Pfeiffer and Kent, 1939).

Mucosal Atrophy

Joske and Blackwell (1959), on the basis of a small series of four patients, suggested that malabsorption of fat after gastrectomy was caused by abnormalities of the jejunal mucosa similar to those seen in coeliac disease. One of their patients showed abnormalities which could well be regarded as those of coeliac disease, two showed slight abnormalities and the fourth was normal. The mucosal appearance of the jejunum is fully considered in Chapter 7, but one or two points should be mentioned here. Shiner (1959) reported 13 normal and 2 abnormal biopsies in post-gastrectomy steatorrhoea. In the Birmingham series, one patient with long-standing idiopathic steatorrhoea also had a duodenal ulcer penetrating the pancreas. Operation was deferred as long as possible for fear of increasing his steatorrhoea. Eventually, a Polya partial gastrectomy was performed and, as feared, his steatorrhoea, which had been mild before, was greatly increased, and diarrhoea became a prominent feature.

Soon after small intestinal biopsy by the oral route became a practicable procedure (Shiner, 1956), attention was drawn to the possibility of steatorrhoea after gastrectomy being due, in some cases, to operation on patients who already had idiopathic steatorrhoea, either latent or with mild symptoms which had escaped proper diagnosis (Paulley, Fairweather and Leeming, 1957). Forshaw (1958) reported a patient with post-gastrectomy steatorrhoea who responded remarkably to a gluten-free diet, as would an adult coeliac, and it seems rational to consider the results of Joske and Blackwell (1959) in these terms especially since, in a much larger series of jejunal biopsies after gastrectomy, mucosal atrophy was quite uncommon (Chapter 7).

Further points in favour of this view are the normal values obtained in absorption tests with folic acid, xylose and glucose after gastrectomy, the absorption of the latter often being enhanced. Further experience with mucosal biopsy and careful clinical trials with gluten-free diets are needed to clear up this point.

SUMMARY

The main conclusions reached from the survey in this chapter may be briefly summarized. The great majority of patients are underweight after gastrectomy because they fail to eat sufficient to maintain or restore weight. In a proportion, there is a loss of calories in the faeces which is mainly due to incomplete digestion of food. Both fat and protein are involved, but dietary loss is not so serious that it could not easily be made up by an increased intake. The best results, nutritionally, are likely to be achieved by operations or re-operations which retain or restore the reservoir capacity of the stomach and allow the patient to eat well, and which retain or restore continuity of the intestinal tract and so maintain, as nearly as possible, the normal mechanisms which control digestion.

A severe malabsorption syndrome after gastrectomy usually denotes a disordered mechanism which, in the absence of pancreatitis, needs to be corrected surgically.

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11

THE OBSERVED METABOLIC CONSEQUENCES OF DIFFERENT UPPER GASTRO-INTESTINAL OPERATIONS

John A. Williams

Any surgeon interested in the surgical treatment of peptic ulceration should attempt to employ an operation which produces the least possible disturbance of upper gastro-intestinal physiology, yet is effective in preventing recurrent ulceration. This chapter describes a search for such an ideal operation and records the observed nutritional defects in patients who have had one of a number of different operations, i.e. vagotomy alone, pyloroplasty, gastro-enterostomy, antrectomy or partial gastrectomy. It is the usual practice today to combine more than one of these procedures in the treatment of chronic ulceration, e.g. vagotomy plus pyloroplasty or vagotomy plus gastro-enterostomy. In order to observe the separate effects of each operation, patients have also been studied who have had vagotomy alone or pyloroplasty alone.

An account of the observed effects of each operation is preceded by a short section summarizing that which has been discussed more fully in previous chapters, concerning the disturbances of physiology consequent upon the operative procedure and the effects which might be expected.

VAGOTOMY

Following the lead of Dragstedt (1935), and beginning in 1947, a series of cases in Birmingham was treated for duodenal ulcer by vagotomy alone, i.e. without a drainage operation (*Figure 63*). Unfortunately, this single therapeutic measure had to be abandoned within two years because of the high incidence of recurrent ulceration or the complications which followed it. However, those patients who remained free from such troubles have given us an opportunity of studying the metabolic results of vagotomy alone. This expression 'vagotomy alone' is stressed because, today, the term 'vagotomy' is often used to mean 'with drainage' by gastro-enterostomy or pyloroplasty. The direct effects of vagotomy alone are reviewed in detail in Chapter 5. They may be summarized as follows.

Reduction of Gastric Acid Production

Production of gastric acid is reduced by abolishing the cephalic phase of gastric secretion (Dragstedt, Harper, Tovee and Woodward, 1947).

Secretion of gastric acid and pepsin is decreased by reducing gastrin production by the antrum and by reducing the gastrin effect on the mucosa of the body (Dragstedt, 1957; Gillespie and colleagues, 1960).

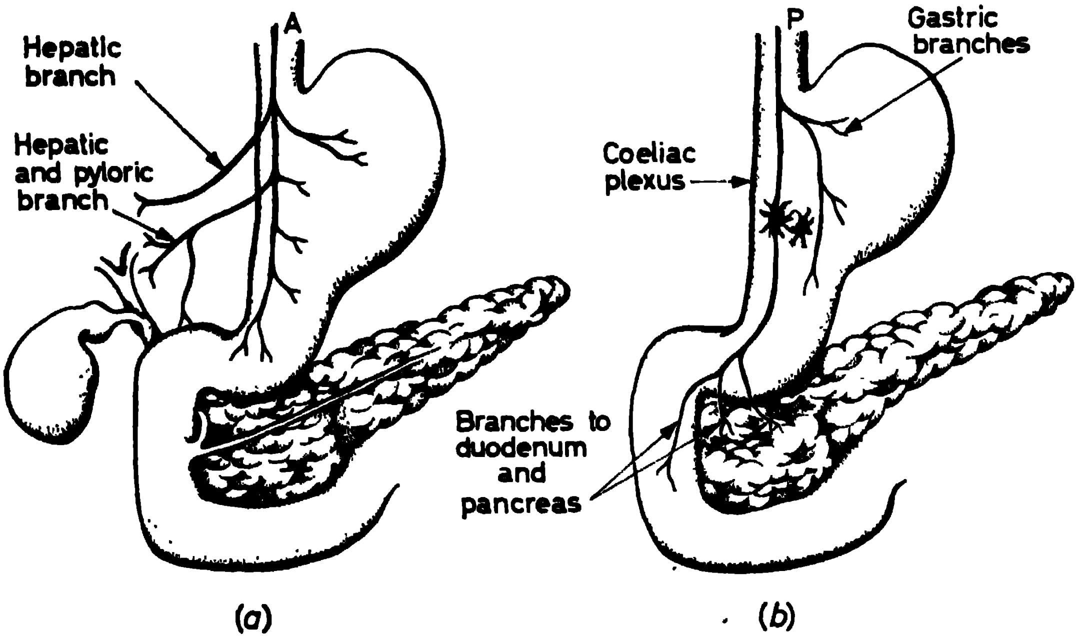

Figure 63. Upper gastro-intestinal distribution of the vagus nerve: (a) anterior vagus (A) supplying stomach liver and biliary apparatus; (b) posterior vagus (P) supplying the stomach and sending a large branch to the coeliac plexus. From this plexus the pancreas, duodenum and most of the rest of the bowel receive their parasympathetic innervation (after Mitchell, 1959)

Temporary Inhibition of Gastric Motility

This leads to gastric retention. After some days or weeks gastric motility appears to return to normal; this is due to intrinsic nervous reflexes and the inherent properties of smooth muscle rather than to a return of vagal innervation. It has been shown that early return of tone does not indicate incomplete vagotomy. The return of 'tone' in the stomach is coincident with the disappearance of some of the unpleasant initial symptoms associated with vagotomy alone, such as foul eructations. The effects of post-vagotomy distension and hypotonia can be minimized or abolished by the addition of a drainage operation. After pyloroplasty of the Weinberg (1957) type, plus vagotomy, many surgeons do not employ any form of gastric decompression—the so-called 'tubeless gastric surgery' (Burge, 1962; Hendry, 1962; Gallagher, 1962). Dragstedt (1962), however, advocates gastric suction for five days, even when a drainage operation is used. This he follows by nightly aspiration of residual juice until gastric motility returns and stasis is abolished: this is usually on or about the eleventh post-operative day.*

Abolition or Impairment of Enterogastric Reflex (*see* p. 112)

When the vagi are cut without a drainage procedure being added, the effect of abolishing the enterogastric reflex cannot be assessed, since the associated gastric hypotonia will cause a marked delay in emptying. However, the effect of vagotomy on this reflex has been nicely demonstrated in man by Waddell and Wang (1953), who found that in the presence of a gastro-enterostomy alone, a fatty meal significantly retarded gastric emptying, but that when a gastro-enterostomy plus vagotomy was performed the retarding effect of fat was lost. The normal role of the vagus in this reflex might be its potentiation of the secretion of enterogastrone by the duodenum in response to fat. The inhibition can, however, be seen to occur before any fat reaches the duodenum. Also, as Hunt (1959 and 1962) has shown, the retarding effect of fat is too rapid in onset and too short in duration to be mediated by a circulating hormone. It would appear from the work of Waddell and Wang (1953) that this loss of retarding effect of fat is a permanent phenomenon and does not return even some months after operation, as does the gastric tone.

Parasympathetic Denervation of the Liver and Biliary Apparatus

In the dog and monkey stimulation of the vagus nerve results in an increased production of bile, contraction of the gall bladder and relaxation of the choledocho-duodenal sphincter (Davenport, 1961). It has been claimed that dilatation of the gall bladder and common duct may occur after complete vagotomy in man (Griffith, 1960 and 1962). Wallace (1960) demonstrated reflux of barium into the common duct during x-ray examination after vagotomy, and

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* Our recent experience, using the one layer Weinberg pyloroplasty plus vagotomy, is that there is usually no significant gastric distension after operation, but that occasionally, unexpected distension may develop, even following the easiest of pyloroplasties. Once distension is allowed to occur it takes many days—sometimes weeks—for motility to return. It seems advisable, therefore, to employ intermittent post-operative gastric suction at least until it is evident that gastric emptying is satisfactory. We now use gastrostomy drainage.

Griffith (1962) quotes Reynolds as reporting 'a definite increased incidence of gall stones after vagotomy'. Bastable (1962) examined the effect of vagotomy on canine biliary and hepatic function. As a result of 25 experiments on five dogs he concluded 'that vagotomy in the presence of pyloroplasty would not alter significantly (1) the gall-bladder contractability; (2) the biliary intraduct pressure; and (3) the maximal secretory pressure of the liver'.

These observations of Bastable are substantiated by observations in man by Glanville (1962) who studied, by cholecystography before and after vagotomy, the size of gall-bladder outline and rate and completeness of emptying. Glanville found that after vagotomy there was no increase in the size of the gall-bladder shadow and the rate of emptying was not significantly different from that before operation.

These observations confirm the impression gained from a few personal studies by cholecystography before and after vagotomy. *Figure 64* shows a normal cholecystogram with normal contraction in response to fat in a patient ten days after a complete truncal vagotomy.

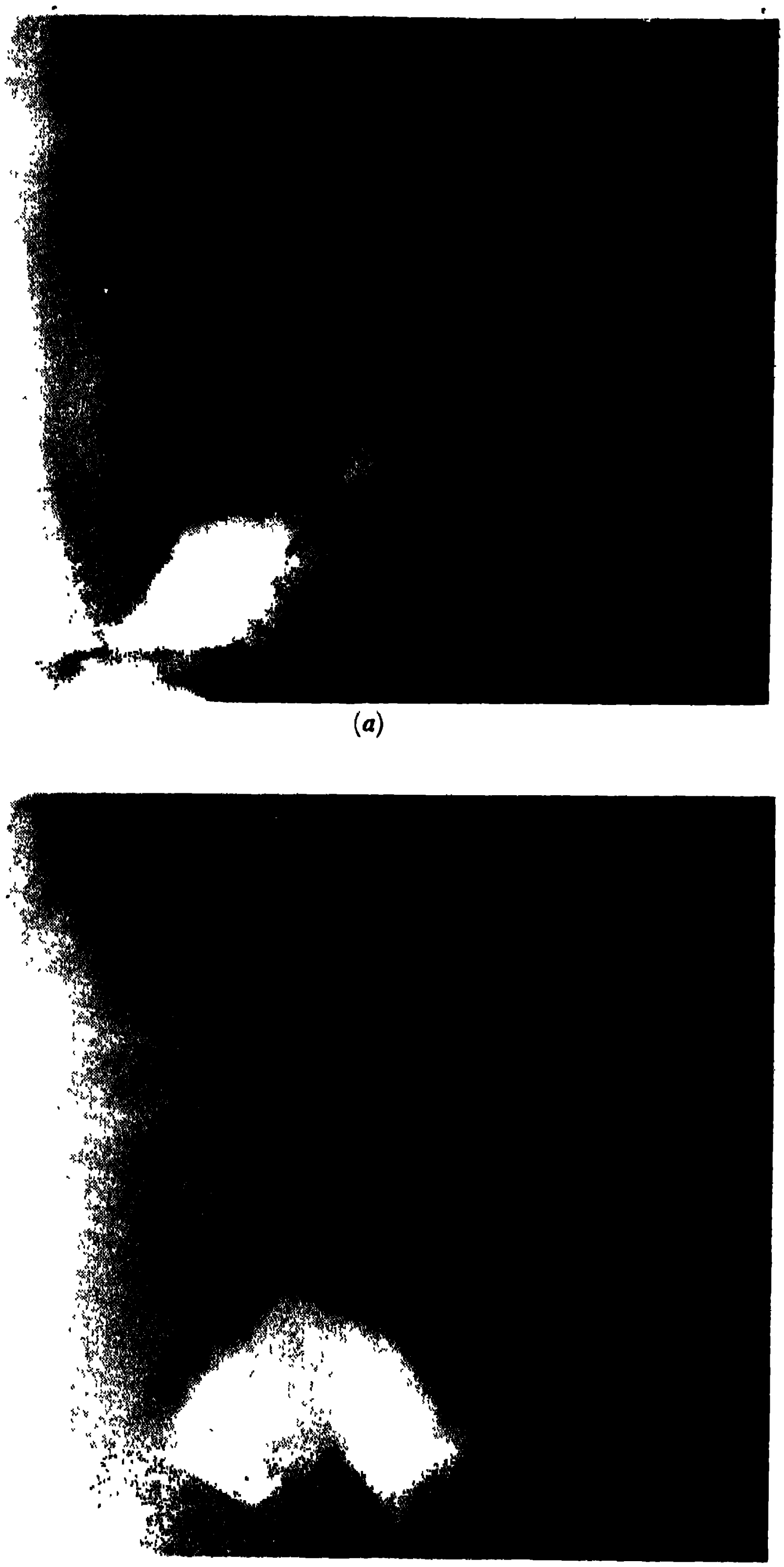
Pancreatic Denervation

Butler (1961) has shown that after vagotomy the response to the stimulus of food in the duodenum or jejunum reveals a reduction in both volume and enzyme content of pancreatic secretion. This work confirms that of Pfeffer, Stephenson and Hinton (1952), who found that after vagotomy both vagal and secretin stimulation of the pancreas were significantly depressed (for a detailed review see Chapter 10, p. 243).

Small Intestinal Denervation

Isaac, Ottoman and Weinberg (1950) observed dilatation and stasis of the small bowel after vagotomy with flocculation of barium, and a slower than normal transit time. As normal small bowel patterns and transit times are commonly seen on x-ray examinations some years after complete vagotomy, these findings of Isaac, Ottoman and Weinberg are either not inevitable or not permanent (*Figure 65*).

The absorption of $Na^{131}I$, glucose and d-xylose was measured in man before, and 18 hours and one week after, vagotomy and pyloroplasty by Cox, Ross and Kay (1962). Although there was an immediate reduction in the rate of absorption this had returned to normal after one week.



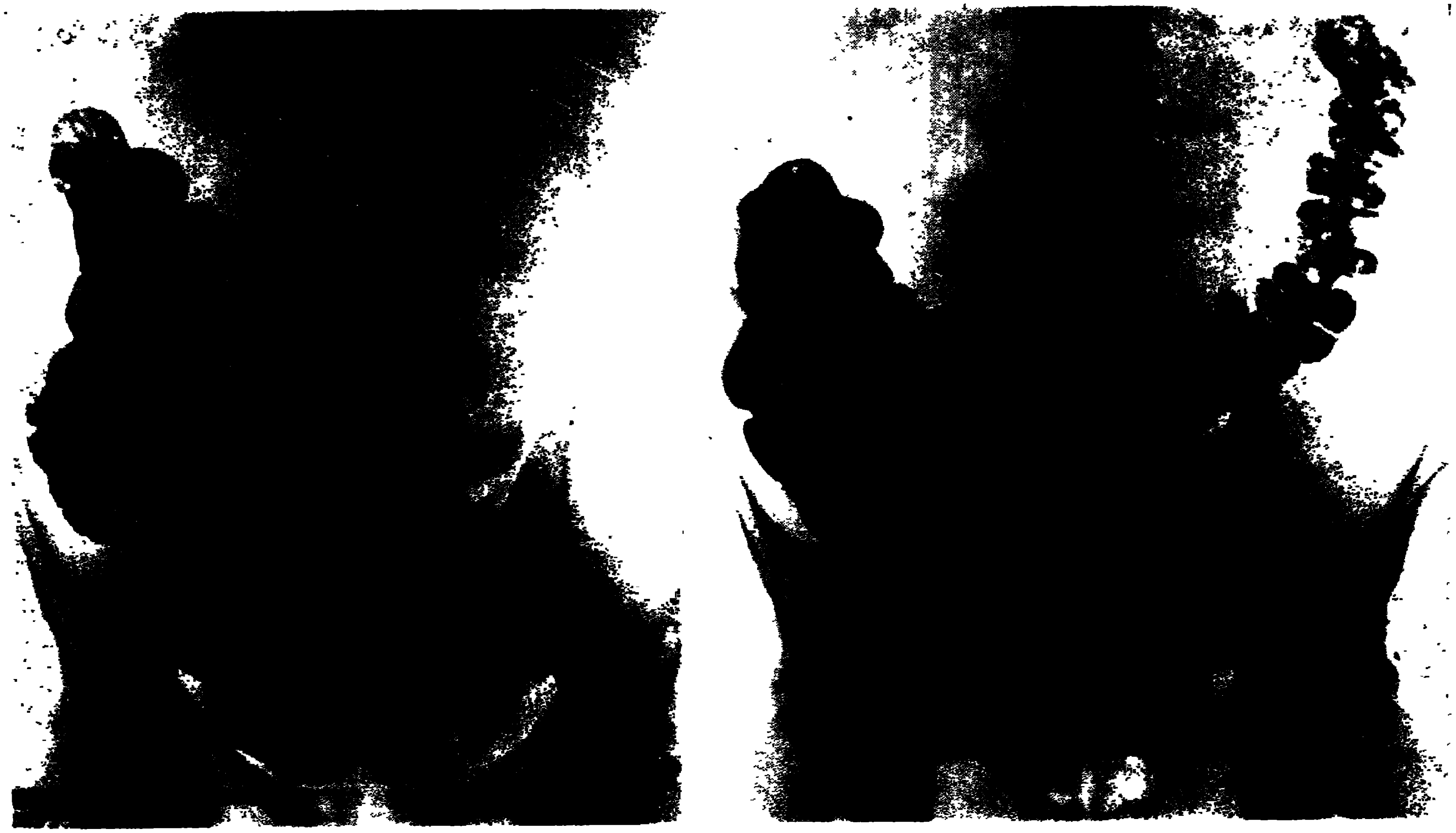
(a)

(b)

Figure 64. Radiographs of cholecystogram taken ten days after a complete vagotomy and pyloroplasty for duodenal ulcer. A normal gall-bladder (a) contracts normally (b) after a fatty meal

(b)

(a)



(c)

(d)

Figure 65. Progression of barium meal through the intestine before [(a) and (c)] and three weeks after [(b) and (d)] pyloroplasty and vagotomy. Films taken 1 h [(a) and (b)] and 4 h [(c) and (d)] after ingestion of meal. There is no significant alteration in the rate of passage through the intestine

In addition to these direct effects of vagotomy, some secondary effects will also influence intestinal function. Decreased acid output following vagotomy does not normally result in a complete achlorhydria but it may do so, particularly if, after denervation, there is prolonged stasis and gastritis leading to atrophy. Achlorhydria would result in impaired gastric homogenization and later might be expected to be followed by diminished intrinsic factor production. Degenerative mucosal changes are, however, less common after vagotomy than gastrectomy (Chapter 6).

Other effects of achlorhydria would be further impairment of pancreatic secretion by the secretin mechanism, and a less efficient absorption of those substances optimally absorbed from the upper small bowel when the pH is low (e.g. iron and calcium). Achlorhydria would also mean a loss of sterilizing effect of the 'gastric acid trap' and therefore a possibility of increased susceptibility to upper intestinal infection.

OBSERVED METABOLIC EFFECTS OF VAGOTOMY

We are currently engaged in a metabolic review of patients 14 or 15 years after having had a vagotomy alone for duodenal ulceration. These investigations will be reported in detail when they are complete, but certain facts of interest have already emerged from 28 studied so far and are pertinent to the present discussion (see Table 14). The completeness of the vagotomy was confirmed by the hypoglycaemia test (Hollander, 1946, Brooke, 1949) performed during the second post-operative year.

From Table 14 it can be seen that, following vagotomy, weight loss, diarrhoea and anaemia are not common. We have not yet studied comparable groups of patients as long as 14 years after partial gastrectomy, but even 5 or 10 years after gastrectomy for duodenal ulcer (see Table 18) the incidence of weight loss, iron deficiency and B_{12} deficiency is significantly higher than it is in the group of patients studied 14 years after vagotomy. Only four of our patients (Nos. 4, 20, 21 and 25) experienced diarrhoea or had more than two stools per day. While one of these patients (No. 4) was ambulant on a 60–80 g fat diet, and still experiencing his customary loose bowel action, a three-day fat balance test showed a daily fat loss of no more than 1·5 g/day.

Steatorrhoea was not suspected in any of the other patients since none had diarrhoea and, on direct questioning, none admitted to noticing bulky floating stools. Three-day faecal fat estimations were made on three more ambulant patients taking a 70 g fat diet. The

TABLE 14

The Effects of Vagotomy Alone

Patient number	*Sex*	*Age*	*Site of ulcer*	*Years since operation*	*Weight loss or gain since operation* lb.	*Present weight below average for age and height*	*Hb*	*Number of bowel actions per day*	*Attacks of diarrhoea*	*Faecal fats* g/day
1	M	52	D	14	+ 39	Yes	13·7	1	No	
2	M	56	D	14	+ 2	No	15·2	1	No	2·5
3	M	52	D	13	− 3	No	15·6	2	No	
4	M	42	D	13	+ 20	No	14·0	1–3	Yes	1·5
5	M	64	D	14	− 4	Yes	16·1	2	No	
6	M	50	D	14	0	No	15·8	1	No	
7	M	51	D	13	+ 2	No	14·5	< 1	No	
8	M	44	D	14	− 1	No	13·4	< 1	No	
9	M	59	D	14	− 3	No	14·6	1–2	No	3·8
10	M	67	D	14	+ 19	No	15·5	1	No	
11	M	59	D	14	+ 67	No	15·2	1	No	
12	M	55	D	14	− 14	No	16·8	1	No	
13	F	58	D	14	− 37	No	13·0	1–2	No	
14	M	48	D	14	+ 7	No	15·8	< 1	No	
15	M	57	D	14	+ 6	No	15·0		No	
16	M	48	D	14	+ 35	No	17·1	1–2	No	
17	M	43	D	13	+ 8	No	14·6	1	No	
18	M	41	D	14	+ 25	No	14·6	1	No	
19	M	50	D	14	+ 14	No	14·3	1	No	
20	F	48	D	13	+ 20	Yes	14·0	1	Yes	1·6
21	M	48	D	14	− 34	Yes	15·5	1	Yes	
22	M	40	D	14	0	Yes	14·6	1	No	
23	M	54	D	15	− 5	Yes	13·7	1	No	
24	M	62	D	13	− 53	Yes	14·3	1	No	
25	M	66	D	14	− 20	Yes	15·6	1	Yes	
26	M	66	D	14	+ 18	Yes	14·6	1	No	
27	M	71	D	14	+ 7	Yes	15·3	1	No	
28	M	62	D	14	+ 14	Yes	16·0	2	No	

mean 24-hour fat excretions were 1·6, 2·5 and 3·8 g, respectively. Our findings are in contrast to the reports by Burge (1960) of a high incidence of post-vagotomy diarrhoea. He describes an incidence of 30 per cent even as late as 5–8 years after operation. It must be emphasized that this complaint of diarrhoea in Burge's series was often only of mild attacks of diarrhoea occurring two or three times a year, such as occurred in our patients (Nos. 4, 21 and 25). These symptoms are more suggestive of increased susceptibility to intestinal infection due to the loss of the gastric acid trap, or to the fact that the associated drainage procedure permitted rapid gastric emptying. When the drainage procedure is a gastro-enterostomy, diarrhoea could be associated with the intestinal cul-de-sac phenomenon (see p. 279). In our patients complete vagotomy has only once (No. 20) been followed by troublesome diarrhoea, and our admittedly few faecal fat estimations confirm the absence of steatorrhoea after vagotomy, as reported by Cox (1961).

Only four patients had lost weight since operation, and three of these were still overweight for age and height, the other, a male of 64, being of a tough wiry build. Of a series of 74 cases treated by the Surgical Unit in Birmingham in 1947–49 by vagotomy alone, 20 recurrent ulcers had been confirmed five years later by operation or by autopsy (Slaney, Bevan and Brooke, 1956) and others have occurred since. These 28 cases are therefore not unselected because they represent those patients who did not have early post-vagotomy complications requiring re-operation.

It is apparent, therefore, that our experience in Birmingham with vagotomy alone suggests that, although there is a prohibitively high incidence of recurrent ulceration after this operation, the successful patients are apparently normal, so far as general nutrition and freedom from anaemia or serious bowel disturbance are concerned. This favourable nutritional state of affairs is in marked contrast with the group studied after partial gastrectomy as reported on pp. 284–287 and in Table 17.

PYLOROPLASTY

In Chapter 5 the pylorus was referred to not as a sphincter but as the distal end of a muscular antrum which may fail to relax before a wave of antral peristalsis and so prevent gastric emptying, the antral contents merely regurgitating back towards the body instead of passing into the duodenum. Destruction of the physiological and anatomical continuity of this pyloric end of the antrum is not, therefore, analogous to the removal of a bung from a barrel when all the contents at once run out. The storage capacity of the fundus for solid foods is relatively unaffected by pyloroplasty; the food still moves gradually into the antrum as in the intact stomach. The length of stay of food in the antrum is presumably shorter after pyloroplasty, although I am not aware of any measurement in man of gastric emptying time after this operation without vagotomy.

Barium studies on children who have had a Ramstedt pyloromyotomy in infancy suggest that, although this operation dramatically relieves the symptoms of congenital hypertrophic pyloric stenosis, it has no lasting effect in altering the rate of gastric emptying from normal (Olnick and Weens, 1949).

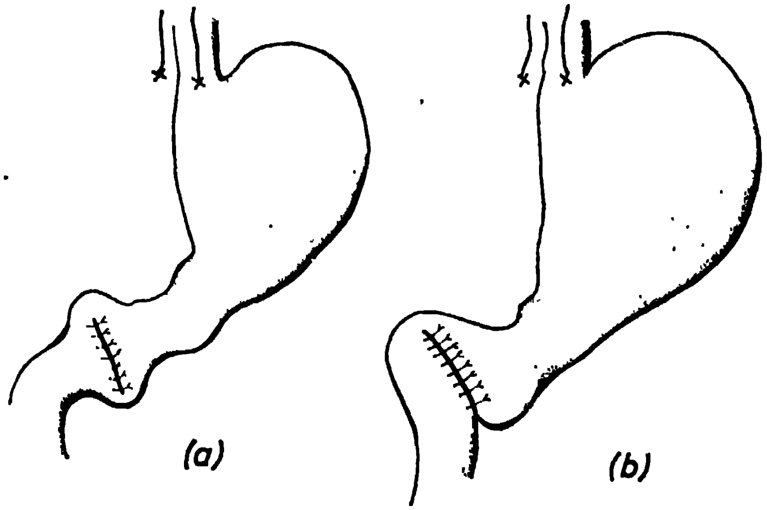


Figure 66. Two types of pyloroplasty or gastro-duodenostomy: (a) Heineke–Mikulicz; (b) Jaboulay–Finney

Pressure studies by Creamer, Cottom and Hindle (1961) have shown that abnormal contractions of the fundus persist for at least ten days after pyloromyotomy for hypertrophic pyloric stenosis in children; future work in this field is awaited with interest.

Radiological follow-up on 95 children, 47 treated surgically and 48 medically, was reported by Andresen (1940). He found that in both groups there was a persistence of the narrowing in the pyloric region for four or more years, but that by adult life all appeared normal. Normal growth and development is the usual consequence of this operation.

The estimations of gastric emptying time in the cases of Andresen (1940) and Olnick and Weens (1949) were not accurately controlled and measured and so cannot strictly be contrasted with the work of Friesen and Rieger (1960) who, basing their opinion on experimental work in man and dogs, suggest that the pylorus plays an important role in regulating gastric emptying. These latter workers found that patients with segmental gastrectomy (*Figure 67*), but without pyloroplasty, had a slower gastric emptying and were less likely to suffer 'dumping' than a comparable group of patients with a Polya-Hofmeister (Billroth II type) gastrectomy. There are, however, very marked physiological differences between the two operations, the segmental gastrectomy leaving behind the vagally denervated antrum as well as the pylorus. Friesen and Rieger found that, in dogs with a segmental gastrectomy, the addition of a pyloroplasty significantly increased the rate of gastric emptying and a liability to experimentally induced 'dumping'. It is not possible, however, to assume from these observations that the role of the normal pylorus has been studied for, as in man, segmental gastrectomy necessarily leads to vagal denervation of the antrum and pylorus. From the work of Friesen and Rieger it can only be assumed that pyloroplasty increases the rate of gastric emptying from the vagally denervated stomach. Further observations are needed to clarify the picture.

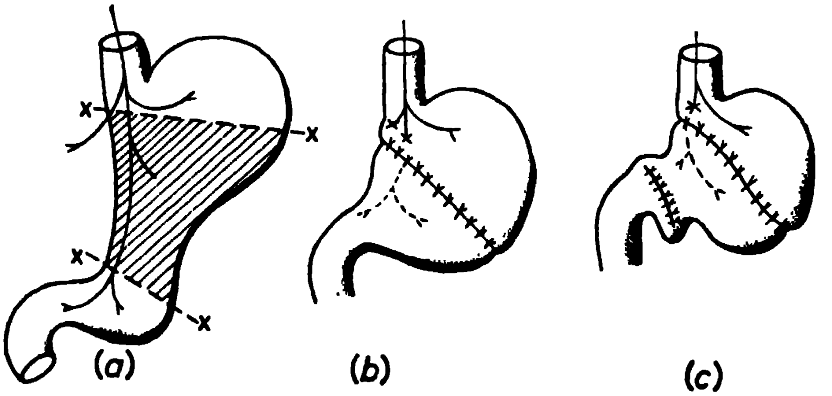


Figure 67. Segmental gastrectomy of Wangensteen (1957). A large area of the acid-secreting body of the stomach is removed (a). This results in vagal denervation of the remaining antrum (b) so that it is necessary to add a pyloroplasty (c)

Does pyloroplasty affect the retarding influence on gastric emptying of fat in the stomach or duodenum, or of hot or hypertonic fluids in the duodenum? Does pyloroplasty result in the passage of incompletely homogenized food into the duodenum? Whatever the answers to these questions it is clear that little demonstrable nutritional ill-effect has been observed from this operation, either in adults or children. We have had the opportunity of studying two patients who, as adults, had a pyloroplasty alone, and three who had pyloroplasty plus vagotomy, all from 6 to 14 years previously. Some of the relevant findings are recorded in Table 15.

TABLE 15

Pyloroplasty Alone

Patient number	*Sex*	*Age*	*Diagnosis*	*Years since operation*	*Weight loss or gain since operation* lb.	*Present weight below average for age and height*	*Hb*	*Number of bowel actions per day*	*Attacks of diarrhoea*	*Dumping*
29	F	60	Old duodenal ulcer	6	+ 14	No	14·6	< 1-2	No	No
30	F	24	Pylorospasm	6	− 32	No	13·8	1	No	No

Pyloroplasty Plus Vagotomy

Patient number	*Sex*	*Age*	*Diagnosis*	*Years since operation*	*Weight loss or gain since operation* lb.	*Present weight below average for age and height*	*Hb*	*Number of bowel actions per day*	*Attacks of diarrhoea*	*Dumping*
31	F	60	Duodenal ulcer	6	− 12	No	13·4	1	No	No
32	F	74	Duodenal ulcer	6	− 4	No	13·8	1	No	No
33	M	59	Duodenal ulcer	14	0	No	15·3	1	No	No

These observations tend to confirm the impression that, in adults, as in infants, pyloroplasty has little demonstrable effect on the patient's nutrition. Patient No. 31 had deliberately lost weight as she was overweight at the time of her original operation; she is still overweight.

The freedom from anaemia and diarrhoea is hardly significant in view of the small numbers involved. Nevertheless, as an assessment of nutritional status the findings after 6–14 years have more meaning than such observations only 2–3 years after operation. We now have a much larger series of patients having had pyloroplasty and vagotomy for duodenal ulceration, and are going to observe with interest their post-operative progress and nutritional status.

GASTRO-ENTEROSTOMY*

The physiological effects of gastro-jejunal anastomoses vary greatly and depend upon a number of factors, including the site of the anastomosis in the stomach and the length of the afferent loop of the jejunum. The two major variations in the gastric siting are shown in *Figure 68*. The different physiological disturbances will be discussed under these two headings, although some are common to both.

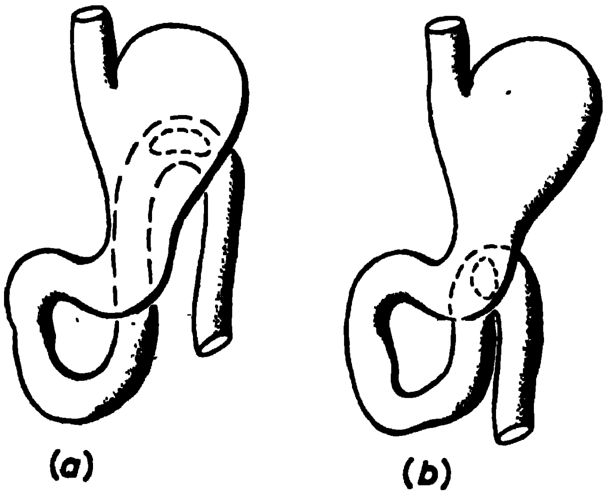


Figure 68. (a) The gastro-jejunal anastomosis is proximal to the antrum—a high gastro-enterostomy; (b) the anastomosis is placed as close as possible to the pylorus—a low gastro-enterostomy

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* Although the jejunum is involved in both types of operation, the expression gastro-enterostomy is used to mean joining the upper jejunum on to the stomach without excision of any part of the latter; gastro-jejunostomy is used to describe the pattern of reconstruction after partial gastrectomy.

HIGH GASTRO-ENTEROSTOMY

Rapid Emptying

If the stoma is placed above the antrum the homogenizing effect of the antrum is lost, as is the regulation of gastric emptying. Food leaves the stomach just as rapidly as is the case following a partial gastrectomy with gastro-jejunostomy.

Recurrent Ulcer

If the antrum is by-passed by the food and gastric secretions, then the antrum is not subjected to the inhibiting effect of acid and the operation shares with other antral-excluding operations the high risk of recurrent ulceration (Nyhus, 1960). This factor of loss of acid inhibition is diminished but not abolished by vagotomy.

Gastro-duodenal Circus

It is not uncommon to find that a patient who has had a gastro-enterostomy many years before, now appears to empty food and gastric juice via the normal route through the pylorus rather than through the stoma. A possible explanation for this phenomenon is that, when the original operation was performed for duodenal obstruction, there was active ulceration with oedema; the effect of the by-pass of food and digestive juices into the jejunum was to allow healing of the duodenal ulcer with subsidence of the associated oedema and the re-opening of the normal route. Antral contractions will tend to drive the chyme in the normal direction and it is not difficult to imagine a circle, which is unphysiological if not vicious, when the duodenal contents re-enter the stomach via the stoma to recirculate through the antrum. This movement can occasionally be seen by fluoroscopy although it is usually obscured by the barium already in the stomach.

The theoretical disadvantages of a high gastric site for a gastro-enterostomy stoma are borne out by the high incidence of ill-effects from this operation. Although this particular siting may not be deliberately planned it is most likely to be performed inadvertently when the stomach is distended, e.g. duodenal obstruction or hour-glass stomach, and hangs down behind the colon.

LOW GASTRO-ENTEROSTOMY

The siting of the stoma near the pylorus is usually effective in preventing most of the complications described above. The stomach usually empties into the jejunum, and the duodenal secretions flow distally to reach the stoma rather than regurgitating back into the stomach through the pylorus. The bathing of the stoma with alkaline juices reduces the risk of jejunal ulceration and the bathing of the antrum in acid secretions ensures the operation of the antral inhibiting mechanism which, in turn, regulates gastric acid production. The retarding effect of fat on gastric emptying is not abolished by a low gastro-jejunostomy when vagal innervation is intact (Waddell and Wang, 1953).

The following are the consequences of any gastro-enterostomy, whether high or low.

Duodenal By-pass

The establishment of a satisfactory gastro-enterostomy results in the delivery of chyme into the jejunum whence it normally flows distally in the efferent loop, only a little passing back into the afferent loop, or by the normal route through the pylorus. Three major effects result from this physiological alteration.

Impairment in Pancreatic Stimulation—Although the pancreas may be stimulated by the cephalic phase of digestion (Davenport, 1961), as a result of gastric distension (White, Lundh and Magee, 1960) or by the presence of food and acid in the upper jejunum (Davenport, 1961), by far the most powerful stimulus for both alkaline and enzyme secretions results from the presence of acid chyme in the duodenum. Butler (1961) has shown that the pancreatic response to food is significantly less when it is in the jejunum than when it is in the duodenum (see Chapter 10).

Impaired Absorption—This might be expected to result from diverting food from the duodenum which has a considerable absorptive capacity. Iron and calcium are both optimally absorbed from the duodenum and progressively less efficiently so as the pH rises lower in the small bowel. It is therefore possible that by-passing the duodenum will adversely affect the absorption of these substances (see Chapters 8 and 9).

In the normal person, much carbohydrate, fat and protein have been absorbed by the time food leaves the duodenum (Borgström and colleagues, 1957), but there is great reserve capacity for the absorption of these substances lower in the alimentary tract which is not impaired by alteration in pH.

Inadequate Mixing of Food With Pancreatic Juice and Bile—This was demonstrated by the elegant intubation studies of Lundh (1958), who studied patients having had a gastro-jejunal anastomosis after partial gastrectomy. As a result of delay in mixing, some pancreatic enzymes may be inactivated before gaining contact with the food. These effects are discussed in greater detail in Chapter 10.

Blind Intestinal Loop

As a result of any form of gastro-jejunostomy, whether performed alone, with vagotomy or as the method of reconstruction after a partial gastrectomy, a loop of bowel is separate from normal alimentary continuity and is a potential blind loop. The ill-effects of small intestinal diverticula and surgically induced cul-de-sacs are well known (Naish and Capper, 1953; Toon and Wangensteen, 1950) and their effects are greater when they occur in the higher reaches of the small bowel. The most satisfactory experimental preparation for the production of this blind loop syndrome is an anti-peristaltic loop high in the jejunum, as created by Toon and Wangensteen (1950) and Cameron, Watson and Witts (1949). The afferent loop of a gastro-jejunostomy (with or without gastrectomy), unlike experimentally produced loops, is not normally a stagnant loop but one which empties itself readily (Card, 1959). At operation on patients with post-gastrectomy syndromes, the afferent loop is usually found to be empty, although sometimes hypertrophied, even where there are symptoms characteristic of afferent loop after a Billroth II type of gastrectomy appears almost invariable and that heavy colonization with certain organisms, particularly loop obstruction. Nevertheless, the studies of Goldstein, Wirts and Kramer (1961) indicate that bacterial colonization of the afferent *E. Coli*, is associated with steatorrhoea. Kinsella, Hennessy and George (1961) described ten cases with afferent loop partial obstruction who were examples of the blind loop syndrome with diarrhoea and malabsorption. Similar examples are recorded in Chapter 4. Bacterial colonization of the afferent loop may be responsible for the impairment of ileal absorption of B_{12} which, in turn, can result in megaloblastic anaemia and occasionally subacute combined degeneration of the cord (a case is described on p. 175) (Naish and Capper, 1953; Starzl, Butz and Hartman, 1961).

The ill-effects of by-passing the duodenum are accentuated if the afferent loop is long, rather than short. Not only is more of the absorptive bowel denied to the digested food, but the likelihood of afferent loop obstruction is greater when the loop is long (Stammers, 1955).

In conclusion it may be said that the physiological alterations resulting from a gastro-enterostomy are much more profound than those following a pyloroplasty, a consideration of some importance when deciding on the type of drainage procedure to employ in combination with a vagotomy.

The results of our findings in ten cases of posterior gastro-enterostomy plus vagotomy of more than five years standing show that half the patients exhibited some abnormality (Table 16). One was underweight and suffered from episodes of diarrhoea, and four were anaemic. One of these, No. 39, had menorrhagia, but in the other three anaemic patients (Nos. 40, 41 and 42) no abnormal blood loss could be detected. No. 40, a 49-year old man, had neither symptomatic nor radiological evidence of stomal ulceration and three successive stools contained no detectable blood. Case 41 had normal periods, but had restricted her diet, avoiding many fruits and vegetables because of post-cibal discomfort. All four anaemic patients responded well to oral iron therapy. Although the numbers are too small to be of statistical significance, these findings do substantiate the belief that gastro-enterostomy plus vagotomy produces physiological disturbances more commonly than does vagotomy or pyloroplasty, alone or in combination. Case 44 is of interest. A sprightly lady of 75, with signs of cervical spondylosis, was referred to an orthopaedic surgeon. On discovering that she was reputed to have had a three-quarter partial gastrectomy in 1931 and, knowing of my interest in post-gastrectomy bone metabolism, he referred her to me for investigation. However, there was no radiological or biochemical evidence of metabolic bone disease. She had no digestive symptoms nor diarrhoea and had not received any medicines since her operation. Her haemoglobin was 12·0 g (82 per cent) and her total iron binding capacity 465 μ/100 ml (normal 350–450 μg), indicating a minor degree of iron deficiency.. Apart from this, no abnormality could be detected (serum vitamin B_{12} 250 μg/ml; serum albumin 4·0 g/100 ml; globulin 3·1 g/100 ml; calcium 9·7 mg/100 ml; phosphorus 3·1 mg/100 ml; alkaline phosphatase 9 units/100 ml; vitamin B_{12} absorption was normal). In view of our experiences with patients ten or more years after partial gastrectomy, we were surprised to find this lady so well nourished after 31 years. She was sure that she had had a partial gastrectomy for 'the surgeon had charged her for one'. We did not, therefore, disillusion her when we performed a barium meal and found an intact stomach with a low gastro-enterostomy.

ANTRECTOMY

Removal of the antrum is an operation which is rarely performed unless it is combined with vagotomy. It is pertinent, however, to consider the physiological effects of antrectomy in order to understand the differences between two commonly employed operations:

TABLE 16

Gastro-enterostomy Plus Vagotomy

Patient number	*Sex*	*Age*	*Site of ulcer*	*Years since operation*	*Weight loss or gain since operation* lb.	*Present weight below average for age and height*	*Hb*	*Number of bowel actions per day*	*Attacks of diarrhoea*
34	M	59	D	15	+ 8	No	15·8	1	No
35	M	60	D	6	− 20	Yes	15·6	2	Yes
36	M	52	D	6	+ 32	No	15·6	1	No
37	M	34	D	6	+ 3	No	15·6	1	No
38	M	33	D	6	+ 5	No	14·3	1	No
39	F	50	D	6	0	No	**11·2**	1	No
40	M	49	D	6	+ 14	No	**7·6**	1	No
41	F	38	D	6	0	Yes	**10·0**	2	No
42	M	67	D	14	− 6	Yes	**6·1**	2	No
43	M	49	D	15	+ 50	No	16·0	3	No

Gastro-enterostomy Alone

44	F	75	D	31	+ 10	No	12·0	1	No

vagotomy plus pyloroplasty, and vagotomy plus antrectomy and gastro-duodenostomy. The reasons for advocating the addition of antrectomy to vagotomy is the alleged higher incidence of recurrent ulcer after vagotomy alone or combined with pyloroplasty or gastro-enterostomy. The two important functions of the antrum are the regulation of acid secretion and the mixing of the food with gastric secretion (see pp. 108–114).

Acid Regulation

Removal of the antrum greatly reduces or abolishes the hormonal phase of gastric secretion since it removes the site of gastrin production. Vagal denervation also reduces gastrin production but it does not abolish it. Gillespie and Kay (1961) report a case in which complete vagotomy (with drainage) reduced the maximal acid output (augmented histamine response) by only 20 per cent instead of the expected 60 per cent. The patient developed a recurrent ulcer within four months of operation which was subsequently cured by antrectomy alone. The augmented histamine response then showed an 88 per cent reduction, which is well within the usual range. Gillespie and Kay therefore postulate that there can be at least two factors operating in producing gastric hypersecretion in cases with duodenal ulcer. The nervous factor is probably the more common and, indeed, vagotomy usually produces a marked and therapeutically effective reduction of gastric acid production. The hormonal (gastrin) factor is well recognized in cases with non-insulin secreting pancreatic adenomata (French and Sircus, 1962), and in some cases of duodenal ulcer the excessive acid secretion may be due to abnormal gastrin secretion by the antrum. If this attractive hypothesis is correct, it is then logical to try to discover a means of detecting the particular factor or factors responsible for gastric hypersecretion in each patient with duodenal ulceration, with the object of being able to select the appropriate operation for that patient and so correct his own physiopathological disturbance. The estimation of the augmented histamine response before and after medical vagotomy (Gillespie and Kay, 1961) is the first step in the application of this hypothesis.

These authors report that, following vagotomy, 5 of their 40 patients did not show the expected reduction in augmented histamine response. One of these was subsequently shown to have an incomplete vagotomy, but in the remaining four a poor response to vagotomy had been predicted because of a similarly poor response to medical vagotomy (hexamethonium and atropine). One of the four patients was the one described above who developed stomal ulceration. It can therefore be deduced that a poor reduction in the augmented histamine response, following medical vagotomy, is an indication to combine antrectomy and vagotomy. Unfortunately, however, as the authors point out, some ten other cases had a poor response to medical vagotomy and yet a satisfactory one to surgical vagotomy. Further work on this subject is awaited with interest.

With perfection of the technique for gastrin assay, it will be of great interest to determine the gastrin content of the antrum in those cases in which the hormonal, rather than nervous, control of gastric hypersecretion appears to predominate.

The regulating effect of the antrum on acid secretion is of first importance when considering the effect of antrectomy for the relief of peptic ulceration; the long-term consequences of the loss of the other antral functions must not be forgotten, however. The thorough mixing of food and gastric secretion, as well as the regulation of the rate of emptying of the food stored in the fundal reservoir, are dependent upon the functional integrity of antrum. Its removal will result in the rapid emptying into the upper small bowel of large particles of food, broken up only by mastication. Whereas the soup-like chyme normally delivered from the intact stomach into the duodenum is mixed with bile and pancreatic secretion by the process of segmentation (see p. 117), the delivery into the upper small bowel of solid lumps of food is likely to precipitate waves of peristalsis sweeping rapidly through the small bowel, an entirely abnormal form of progression in the small bowel and one which will result in so-called 'intestinal hurry'.

The lack of regulation of gastric emptying will also predispose to the dumping syndrome. Herrington (1962) states that 30 per cent of patients experience dumping after vagotomy and antrectomy followed by gastro-jejunostomy, but that if the anastomosis is by gastro-duodenostomy there will be a lesser incidence of dumping and no case of severe dumping. In an attempt to devise an operation which would retain the physiological effects of an innervated antrum, yet reduce the acid-producing area of the stomach, Wangensteen (1940) revived Connell's (1929) earlier conception of a tubular resection of a large part of the acid-producing part of the stomach (*Figure 69*).

The operation of tubular gastrectomy proved unacceptable as a form of treatment for duodenal ulceration because of the high rate of recurrent ulceration (Wangensteen, 1957; Nyhus and colleagues, 1960). This failure was due, partly, to the continued gastrin release from the innervated antrum. However, apart from its inacceptibility because of recurrent ulceration, this operation appeared to be less disturbing, metabolically, than operations in which the antrum was either removed (Billroth I or Billroth II partial gastrectomies) or denervated (segmentary gastrectomy). MacLean (1954) reports a follow-up of 35 cases, of which 14 had either Billroth I or Billroth II partial gastrectomies, 16 segmental resections and 5 tubular resections. Unlike the other groups, the patients after tubular resection did not suffer weight loss and had a normal faecal fat excretion. The number of cases is too small to permit us to draw firm conclusions.

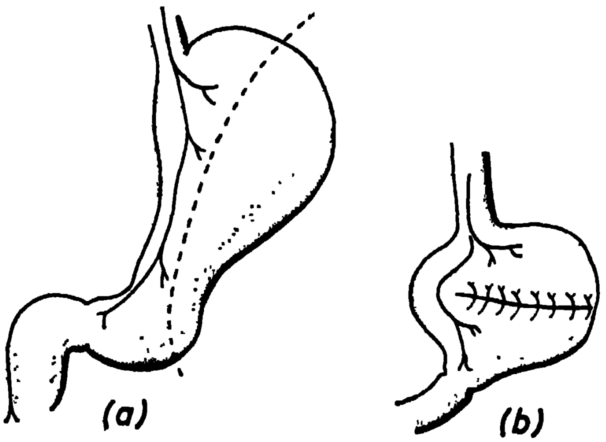

Figure 69. Tubular gastrectomy of Wangensteen (1940 and 1957). A large area of the acid-secreting body is removed and a vagally innervated antrum remains

As yet, we have not followed any cases for more than two years after the operation of vagotomy and antrectomy, so no comparison can be made between these patients and those having had other operations many years before. A small personal series of eight cases of vagotomy and antrectomy with gastro-duodenal anastomosis has now been followed-up for 2 years and there is no evidence of anaemia (all cases are on oral iron). Only one patient has lost weight, and he now has attacks of diarrhoea. Pre-operative faecal fat excretion in this man was 9·0 g/day and after operation it was 11·0 g/day. Three others have experienced dumping, one of whom is still moderately incapacitated.

PARTIAL GASTRECTOMY

The standard operation of partial gastrectomy performed in most centres in this country today involves the removal of approximately 7/10ths or more of the stomach but, as Harkins laments, few surgeons make more than a rough estimate of the amount removed (Olch and Harkins, 1960). The physiological disturbances resulting from this operation are, in effect, the sum of those described under the previous headings. The pylorus, the antrum and part of the body are removed and often the vagi are divided, sometimes including the hepatic and coeliac branches. Most important of all, gastrojejunal anastomosis by-passes the duodenum and creates a blind duodenal loop.

Of those disturbances mentioned previously, the only one which is not always produced by partial gastrectomy is that of total abdominal vagotomy. Recapitulating, the main physiological disturbances which may be expected to follow any form of partial gastrectomy, are:

(1) Reduction of the storage capacity of the body and fundus.
(2) Reduction of acid–pepsin production which, combined with the loss of the triturating effect of the antrum, leads to a much less efficient breakdown of particles of food.
(3) Loss of the pyloric regulating mechanism, so that hot, hypertonic and fatty foods are not retained in the stomach remnant but pass *en masse* into the small bowel.
(4) Impairment of the secretion of bile and pancreatic juices because, in place of small boluses of acid chyme arriving in the duodenum at regular intervals, a neutral or less acid heterogeneous mass arrives in the same form as it is eaten; this is to the detriment of the secretin-pancreozymin mechanisms.
(5) The rapid passage of hypertonic solutions and carbohydrate foods into the upper small bowel will tend to give rise to 'dumping'.
(6) Absorption of iron and calcium is impaired as a result of decreased acidity and of by-pass of, or rapid passage through, the duodenum.
(7) The secondary gastric mucosal atrophy, which follows gastric operations, may lead to impaired secretion of intrinsic factor, and consequent malabsorption of vitamin B_{12}.
(8) These degenerative changes in the gastric mucosa may possibly be precancerous.
(9) The removal of the gastric acid trap, which sterilizes food and helps to prevent the bacterial colonization of the upper gastrointestinal tract.

In addition, there are disturbances which are specific to the Billroth II gastrectomy with its gastro-jejunostomy and blind afferent loop.

(10) By-passing the duodenum impairs the secretion of pancreatic juice and the discharge of bile, while the mixing of these juices and the food is hindered.

(11) The creation of a blind loop of duodenum, in which bacterial colonization may occur, will impair the absorption of fats, vitamin B_{12} and, possibly, other substances.

This formidable list might be called 'the eleven reasons why one should think seriously before deciding to operate upon a person with a peptic ulcer'.

It is surprising that, with such profound physiological consequences, partial gastrectomy does, in fact, prove such a satisfactory operation in the majority of cases. How satisfactory is it? It is recorded in Chapter 2 that, in the series of 955 cases from the Surgical Professorial Unit in Birmingham, recurrent ulceration occurred in only 2 per cent of cases; this fact alone is a source of considerable satisfaction to both patient and surgeon. However, weight loss, anaemia and diarrhoea occur in a disturbingly high proportion of cases. The series of 100 unselected cases five years after partial gastrectomy, studied by us (Jones and colleagues, 1962) to determine the incidence of many of the nutritional deficiencies, has been used as a basis for discussion and opinion in the chapters on anaemia, intestinal mucosal changes and bone metabolism. These data will not be presented again here except in so far as it allows comparison with data presented in Tables 14–17. Table 17 summarizes the findings in our cases studied after Billroth I and Billroth II gastrectomies.

TABLE 17

Comparison of Observed Effects in Patients 5–6 Years After Partial Gastrectomy for Gastric and Duodenal Ulceration

Type	*Mean age*	*Proportion below pre-operative weight* per cent	*Proportion below optimum weight* per cent	*Proportion with anaemia* per cent		*Proportion with diarrhoea* per cent
				Men	*Women*	
Billroth I for gastric ulceration	59	25	57	38·5	25	2
Billroth II for duodenal ulceration	55	34·5	55	29	38·5	3

There is no statistical significant difference between any of the measurements of the two groups. The effects on calcium metabolism and bone disease of partial gastrectomy and vagotomy have been discussed in Chapter 9 (pp. 207–209). It is seen there that there is a significantly higher incidence of bone disease after partial gastrectomy than after vagotomy. The observed effects of partial gastrectomy on protein metabolism as indicated by the serum albumin level are shown in *Figure 70.*

It will be seen that eight patients had a serum albumin level below 4·0 g/100 ml, but in none was the level below 3·0 g/100 ml.

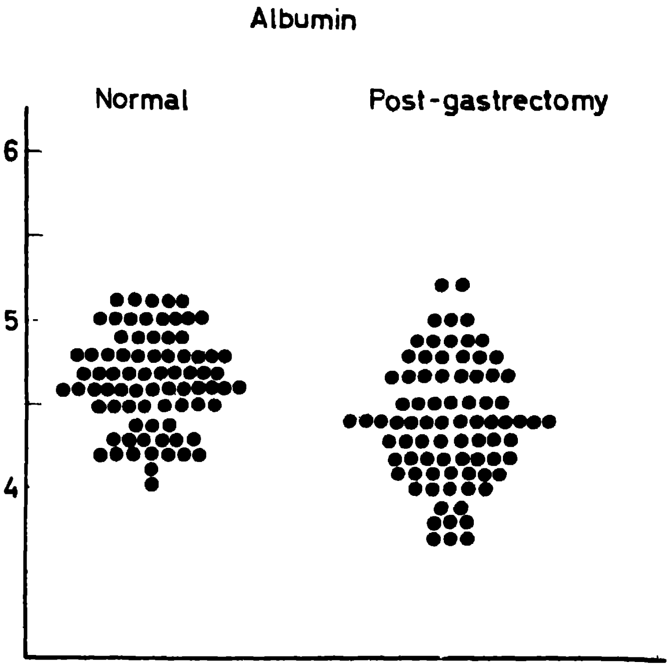

Figure 70. Scatter diagram of serum albumin levels (in g/100 ml) in healthy controls and 74 patients, 5–6 years after partial gastrectomy

Similar minor depressions of the serum albumin level have been seen in patients after other upper gastro-intestinal operations, but the numbers are too small to give significance to any comparison.

SUMMARY

As this study refers to results observed in a small number of patients, particularly in the groups with pyloroplasty and gastro-enterostomy, it is not possible as yet to give any fully substantiated opinions.

What is clear, however, is that very little metabolic upset results from the operation of vagotomy alone, or combined with pyloroplasty, providing that it is not followed by recurrent peptic ulceration. Anaemia is very uncommon. Weight loss after operation occurs in only 14 per cent of cases. Evidence of disturbance of calcium metabolism is present in 12 per cent of patients 12–14 years after operation and diarrhoea occurs in 14 per cent. In contrast, after partial gastrectomy, weight loss is significantly more common even

TABLE 18

Operation	*Storage*	*Homogenization*	*Periodic dispensing through pylorus*	*Pancreatic and biliary stimulation*	*Duodenal mixing of food and ferments*
Vagotomy	Unaffected	Not affected, except for early diminished antral movement	Retarded	Possibly slightly reduced	Unaffected
Pyloroplasty	Unaffected	Diminished. Increased rate of emptying	Slight increase in rate of emptying	Probably unaffected	Probably unaffected
Gastro-enterostomy	Unaffected	Diminished. Increased rate of emptying	Steady loss from stomach	Considerably reduced	Abolished
Tubular gastrectomy	Reduced	Unaffected	Unaffected	Reduced due to reduced acidity	Unaffected
Partial gastrectomy (Billroth I)	Reduced	Grossly impaired	Rapid loss of food from body of stomach	Reduced. Less acid and more rapid passage	Impaired
(Billroth II)	Reduced	Grossly impaired	Very rapid onward passage of meal	Considerably reduced	Abolished

five years after operation. Anaemia is found in approximately 30 per cent of cases, but post-operative diarrhoea is less common than after vagotomy.

In the series reported here, there is no significant difference in the metabolic status of patients after a Billroth I operation, compared with those after a Billroth II. This does not necessarily mean that the Billroth II operation does not produce more metabolic defects since, in this series, the Billroth I operations were performed for gastric ulceration, a condition which at the time of operation is usually associated with a greater incidence of nutritional disturbance.

The effects of different observations on some of the important physiological functions of the upper gastro-intestinal tract are summarized in Table 18.

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12

CONCLUSIONS

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When discussing the recognized post-gastrectomy syndromes, efferent loop obstruction, and diarrhoea and anaemia, it was stated that treatment by conversion to a Billroth I type of reconstruction plus vagotomy relieved most of them; Table 1, analysing our experience with 61 cases, bears out this statement. One might, at first, question whether such different symptom patterns could be benefited by the same operation, but when one realizes that all genuine post-gastrectomy complaints are associated with four fundamental factors, namely: (*a*) small stomach reservoir; (*b*) delivery of undigested, hypertonic food directly into the upper jejunum; (*c*) the presence of an afferent loop, thus by-passing the duodenum; and (*d*) the absence of antral and pyloric mechanisms, one can appreciate that any procedure that eliminates one or more of these factors will almost certainly help the patient. The Billroth I type of operation does not employ an afferent loop at all and, compared with a Billroth II operation, retards the rate of deposit of almost wholly undigested food in the jejunum. Moreover, food is mixed with bile and pancreatic juices more thoroughly than is possible after the Billroth II gastrectomy. Admittedly, in the absence of a pyloric mechanism, food still reaches the upper jejunum earlier and in a less well prepared state than normal, and these factors probably account for such 'dumping' as the Billroth I patients suffer, but it is usually of a less severe nature than in the Billroth II patients. Also, as Butler (1961) has shown, pancreatic secretion is more nearly normal after gastro-duodenostomy than after gastro-jejunostomy. It is not surprising, therefore, that the incidence of all post-gastrectomy syndromes, as well as metabolic disturbance, is lower after the Billroth I operation than after the Billroth II procedure.

The main anxiety in the treatment of duodenal ulceration is the possible development of recurrent or stomal ulceration, yet it has been shown (Harkins and colleagues, 1953) that this risk is reduced by adding vagotomy, and an increasing number of reports show that such undesirable sequelae as may follow the Billroth I operation plus vagotomy, are less than after gastro-jejunostomy (Cox and Kerr, 1957).

Many surgeons today maintain that partial gastrectomy of the Billroth II type is an extremely good operation, quite the best for preventing further ulceration, and satisfying over 80 per cent of patients. In many ways this is true. Nevertheless, everything that has been recounted in this book points to the desirability of adopting something less disturbing, physiologically, than removal of three-quarters of the stomach and joining the remnant to the jejunum provided that such an operation is equally effective in the prevention of future ulceration. At the same time, it must carry a lower incidence of post-operative discomforts and nutritional sequelae. The complications which can at least in part be attributed to the joining of stomach stump to the jejunum, thereby creating an afferent loop and by-passing the duodenum, are as follows:

(1) Disturbance of fat metabolism, sometimes leading to diarrhoea, and often contributing to malnutrition.
(2) Iron deficiency, since the optimum site of iron absorption is by-passed. Increased intestinal blood loss may also occur.
(3) Deficient calcium absorption.
(4) Infection of the 'blind' afferent loop, particularly if its drainage is impaired. The contained organisms contribute to the malabsorption of fats and vitamin B_{12} as well as to loss of protein.
(5) An incidence of dumping.
(6) Mechanical embarrassment of the afferent loop leading to afferent loop syndrome and other phenomena.
(7) Mechanical embarrassment of the efferent loop, particularly when it is crowded beneath the meso-colon in the retro-colic anastomosis. These embarrassments may lead to a subacute, high small bowel obstruction.

Much has been written of late in favour of vagotomy and antrectomy, although even with this operation some workers advocate reconstruction by gastro-jejunostomy. The advocacy of such a reconstruction is surprising since it introduces the need for an afferent loop with all its disadvantages. It would be more physiological to anastomose the stomach remnant to the duodenum.

Quite the nearest-to-normal arrangement would seem to be that which follows vagotomy and pyloroplasty or anterior pylorectomy, since this leaves a normal reservoir, permits food to pass by the normal route, thereby allowing admixture with bile and pancreatic secretions, eliminates the evils of the afferent loop, and leaves part of the antro-pyloric mechanism.

With vagotomy and pyloroplasty the operative mortality is less than after partial gastrectomy, the serious immediate post-operative complications are fewer and the incidence of subsequent post-prandial discomforts is considerably lower. Following vagotomy and pyloroplasty the function of the antrum (see Chapter 5) begins to return spontaneously within a few days. In a small proportion of cases, however, the immediate post-operative course may cause a little anxiety because of gastric retention. This is not entirely or necessarily due to oedema at the site of the pyloroplasty, but would appear to result from physiological obstruction by the whole antrum which, for several days, remains in a state of either spasm, inco-ordination or inertia. In such cases, as much as 1–2 l. may be aspirated per day up to the fifth or sixth day or, very occasionally, for much longer. If the naso-gastric tube is withdrawn, vomiting develops or, very rarely, a state akin to acute dilatation of the stomach, with paresis and dilatation of the small intestine. With precautions against these unusual possibilities, such complications can be circumvented. Dragstedt (1962) advocates leaving the naso-gastric tube in position for five days and, after that, passing a tube each evening to assess and remove any retained fluids. Others employ a drainage gastrostomy as a routine. In our experience an awareness of the possibility of, and a readiness to use, the more prolonged aspiration, as advocated by Dragstedt, has been successful in restoring full function. One of our cases mentioned in Chapter 11 took three weeks to settle. Holt, at the 1962 Meeting of the Association of Surgeons of Great Britain and Ireland, reported most favourably on a series of patients treated for duodenal ulcer by this operation; and earlier the same year he published a ten-year follow-up on 100 patients treated by vagotomy and gastro-enterostomy (Holt and Lythgoe, 1962). Our own results in a smaller series of patients treated by vagotomy and pyloroplasty are as promising as those of Holt.

What remains to be seen is the incidence of stomal ulceration in our patients. Our experience with vagotomy alone was one of a prohibitively high recurrent ulcer rate (Slaney, Bevan and Brooke, 1956). Burge (1959) reports a recurrence rate of 3·1 per cent after vagotomy and pyloroplasty which is very significantly higher than that of 0·5 per cent after vagotomy plus antrectomy published by Harkins and colleagues (1960). It is possible that removal of the antrum will prove to be the best device for preventing recurrent ulcer after vagotomy, but one will probably have to pay the price of a higher operative mortality and a higher incidence of dumping and of metabolic disturbance than occur after pyloroplasty.

For the past two years we have been employing vagotomy combined with pyloroplasty, or with antrectomy and gastro-duodenostomy in the treatment of duodenal ulceration. We are following our patients with special reference to their subsequent nutritional status, but some years must elapse before we can give an opinion about the rival merits of the two operations in our hands.

As pointed out in the earlier part of this work, there are thousands of patients throughout the world today suffering from some form or other of post-gastrectomy ill-health in the form of gastro-intestinal symptoms or metabolic disorders. One realizes that about nine times this number are well content with the result of their operation. But this is no excuse for not enquiring into the reasons why 50 per cent suffer the symptoms of anaemia, 40 per cent are below weight and rather more than 10 per cent continue with or develop further discomforts. If possible, therefore, we must try to find an operation with a lower incidence of undesirable sequelae. We already know the fundamental causes for many of the post-gastrectomy discomforts and are now learning the mechanisms of the metabolic consequences.

It is our duty not only to adopt the least physiologically disturbing operation, but also to prevent the development of nutritional deficiencies in those patients who already have had one of the more disturbing procedures. Such preventive measures will include advice about diet and size and number of meals, and also the regular supplementation of those minerals and vitamins which, as a result of their operation, they may no longer be able to absorb in adequate amounts. The patient's own medical attendant is the best person to undertake this supervision, because continued follow-up at hospital is liable to engender a spirit of invalidism. Such supervision need be no more than once a year, and at each visit the weight and, where possible, the haemoglobin should be recorded. Simple advice will usually help to minimize such symptoms as mild dumping, and to prevent weight loss. Ensuring that the patient has sound teeth or well fitting dentures and masticates thoroughly before swallowing, will help to reduce some of the ill-effects following removal of the antrum. This advice should be given in such a manner as not to make the patient unnecessarily concerned about himself, and in particular should encourage him to eat as normal and varied a diet as possible. It is difficult to lay down a precise programme concerning the regular supplementation of minerals and vitamins, since conditions of medical practice vary so much in different parts of the world. The ideal permanent daily supplement would certainly include iron, calcium and vitamin D. Injections of vitamin B_{12} are not indicated for prophylactic purposes and should be prescribed only after a precise diagnosis of vitamin B_{12} deficiency.

For all our patients who have had a partial gastrectomy we prescribe ferrous sulphate 200 mg and, because a patient rendered hypochlorhydric by the operation may not tolerate or absorb this iron as well as normal, ascorbic acid 200 mg in addition. We also prescribe the B.P.C. preparation of 'calcium with vitamin D' tablets containing approximately 500 mg of calcium lactate, 150 mg of calcium phosphate and 500 units of vitamin D. All these supplements should be taken once a day, conveniently on retiring to bed. It is important to avoid prescribing large doses of vitamin D because of the dangers of vitamin D poisoning.

Practical difficulties may make it impossible to take these items regularly each day, and it may also be objected that such regular medication will engender the very spirit of invalidism which we are trying to avoid. How these difficulties are resolved depends upon the particular circumstances of each case, but where regular supplementation is not possible we certainly recommend that, in addition to a yearly check of weight and haemoglobin level, arrangements be made for a full haematological examination, including serum levels of vitamin B_{12} and alkaline phosphatase at approximately five-yearly intervals. The earliest signs of deficiency demand immediate treatment. We do not advise any dietary supplements for patients who have had a vagotomy and pyloroplasty.

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